

GenCore version 5.1.9
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OM protein - protein search, using sw model

Run on: September 21, 2006, 14:40:07 ; Search time 0.001 Seconds
(without alignments)
984.233 Million cell updates/sec

Title: US-10-668-178-2
Perfect score: 780
Sequence: 1 VRSSRTPSDXPVAHVANP.....RPDYLDPAESGQVYFGIIAL 157

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 40 seqs, 6269 residues
Total number of hits satisfying chosen parameters: 40

Minimum DB seq length: 0
Maximum DB seq length: 2000000000
Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 500 summaries

Database : xedit-findpat.subdb: *

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	773	99.1	157	1	ADH10160 Human tumour necro
2	766	98.2	157	1	ADH10160 TNF-R1 specific hu
3	765	98.1	157	1	ADH10160 TNF-R1 specific hu
4	764	97.9	157	1	ADH10160 TNF-R1 specific hu
5	762	97.7	157	1	ADH10160 TNF-R1 specific hu
6	759	97.3	157	1	ADH10160 TNF-R2 specific hu
7	758	97.2	157	1	ADH10160 TNF-R1 specific hu
8	754	96.7	157	1	ADH10160 TNF-R2 specific hu
9	752	96.4	157	1	ADH10160 TNF-R2 specific hu
10	751	96.3	157	1	ADH10160 TNF-R1 specific hu
11	751	96.3	157	1	ADH10160 TNF-R1 specific hu
12	751	96.3	157	1	ADH10160 TNF-R2 specific hu
13	750	96.2	157	1	ADH10160 TNF-R2 specific hu
14	750	96.2	157	1	ADH10160 TNF-R2 specific hu
15	749	96.0	157	1	ADH10160 TNF-R2 specific hu
16	749	96.0	157	1	ADH10160 TNF-R2 specific hu
17	749	96.0	157	1	ADH10160 TNF-R2 specific hu
18	749	96.0	157	1	ADH10160 TNF-R2 specific hu
19	749	96.0	157	1	ADH10160 TNF-R2 specific hu
20	749	96.0	157	1	ADH10160 TNF-R2 specific hu
21	749	96.0	157	1	ADH10160 TNF-R2 specific hu
22	748	95.9	157	1	ADH10160 TNF-R2 specific hu
23	748	95.9	157	1	ADH10160 TNF-R2 specific hu
24	748	95.9	157	1	ADH10160 TNF-R2 specific hu
25	748	95.9	157	1	ADH10160 TNF-R2 specific hu
26	747	95.8	157	1	ADH10160 TNF-R1 specific hu
27	747	95.8	157	1	ADH10160 TNF-R2 specific hu
28	747	95.8	157	1	ADH10160 TNF-R2 specific hu
29	746	95.6	157	1	ADH10160 TNF-R2 specific hu
30	746	95.6	157	1	ADH10160 TNF-R2 specific hu
31	746	95.6	157	1	ADH10160 TNF-R2 specific hu
32	746	95.6	157	1	ADH10160 TNF-R2 specific hu
33	744	95.4	157	1	ADH10160 TNF-R1 specific hu

34	743	95.3	157	1	ADH10160 TNF-R1 specific hu
35	743	95.3	157	1	ADH10160 TNF-R1 specific hu
36	742	95.1	157	1	ADH10160 Human TNF-alpha mu
37	741	95.0	157	1	ADH10160 TNF-R1 specific hu
38	741	95.0	157	1	ADH10160 Human TNF-alpha mu
39	741	95.0	157	1	ADH10160 TNF-R1 specific hu
40	698	89.5	146	1	ADH10160 TNF-R1 specific hu

ALIGNMENTS

RESULT 1
ADH10160
ID ADH10160 standard; protein; 157 AA.

XX AC ADH10160;

DT 11-MAR-2004 (first entry)

XX DE Human tumour necrosis factor variant protein.

XX KW TNF: tumour necrosis factor; polyethylene glycol; cytostatic; cancer;
human; variant.

XX OS Homo sapiens.

XX PN EPI354893-A2.

PD 22-OCT-2003.

XX 30-JAN-2003; 2003EP-00250587.

PR 25-MAR-2002; 2002JP-00083509.

PR 26-JUN-2002; 2002JP-00185387.

XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.

PA (MAYU/) MAYUMI T.

PA (TSUT/) TSUTSUMI Y.

PA (NAKA/) NAKAGAWA S.

XX Mayumi T, Tsutsumi Y, Nakagawa S, Ikegami H;

XX WPI; 2004-063952/07.
N-PSDB; ADH10169.

XX A physiologically active complex which comprises a protein part with
tumour necrosis factor activity and a high molecular part has higher
stability and retention in living bodies and is useful to treat disease,
particularly cancer.

XX Example 1; SEQ ID NO 3; 18pp; English.

XX The present sequence represents a physiologically active complex which
comprises a proteinaceous part with tumour necrosis factor (TNF) activity
and a high molecular part bound artificially to the N-terminus of the
proteinaceous part. The proteinaceous part comprises the sequence
selected from ADH10159 and the molecular part has a molecular weight of
500-5000 Da and is a homopolymer of polyethylene glycol or a copolymer of
ethylene glycol and its derivatives. The invention is used to treat
susceptible disease, particularly cancer. The complex has a higher
stability and longer retention time in living bodies than intact tumour
necrosis factor. The present sequence represents a human TNF variant
protein.

XX Sequence 157 AA;

Query Match 99.1%; Score 773; DB 1; Length 157;

Best Local Similarity 96.2%; Pred. No. 0;

Matches 151; Conservative 0; Mismatches 6; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAHVANPQAEQQLQNLNRRALLANGVELDQNLVPSGGLYLIYS 60

```

Db      1 VRSSRTSPDMPVHVHVANPQAEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
Qy      61 QVLFXGQGCSTHLLTHITISRIASVYQTXVNLLSAIXSPCQRETPEGAXPMYEPYIL 120
      |||||
Db      61 QVLFSGQGCSTHLLTHITISRIASVYQTPVNLLSAIRSPCQRETPEGAXPMYEPYIL 120
Qy      121 GGVFQLEKGDRLSAEINRPDYLDPAESGQVYFGIIAL 157
      |||||
Db      121 GGVFQLEKGDRLSAEINRPDYLDPAESGQVYFGIIAL 157

RESULT 2
ID      AEB45433 standard; protein; 157 AA.
XX
AC      AEB45433;
XX
DT      22-SEP-2005 (first entry)
XX
DE      TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:17.
XX
KW      tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW      autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW      acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW      plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
KW      antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW      antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW      vasotropic; cerebroprotective; dermatological; immunomodulator;
KW      antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW      mutein.
XX
OS      Homo sapiens.
OS      Synthetic.
XX
PN      WO2005066206-A1.
XX
PD      21-JUL-2005.
XX
PF      05-JAN-2005; 2005WO-JP0000032.
XX
PR      06-JAN-2004; 2004JP-00001427.
XX
PA      (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA      (MAYU)/ MAYUMI T.
PA      (TSUT)/ TSUTSUMI Y.
PA      (NAKA)/ NAKAGAWA S.
XX
PI      Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
DR      WPI; 2005-506850/51.
XX      N-PSDB; AEB45447.
XX
PT      Novel tumor necrosis factor TNF mutant protein, useful for treating
PT      and/or preventing diseases such as inflammation, and other diseases
PT      caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT      rheumatoid arthritis, allergy.
XX
PS      Claim 4; SEQ ID NO 17; 34pp; Japanese.
XX
CC      The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC      particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC      TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC      a TNF mutant protein comprising an amino acid sequence derived from the
CC      human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC      one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC      N-terminus, and amino acid residues at positions 84-89 by other amino
CC      acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC      mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC      protein. The TNF mutant proteins are useful for treating and/or
CC      preventing diseases such as inflammation, and other diseases caused by
CC      overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC      cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC      Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,

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CC      transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC      respiratory syndrome (SARS), atherosclerosis, Bence's disease, systemic
CC      lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC      etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC      represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
CC      The sequence data for this patent did not form part of the printed
CC      specification, but was obtained in electronic format directly from WIPO
CC      at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ      Sequence 157 AA;

Query Match      98.2%; Score 766; DB 1; Length 157;
Best Local Similarity 94.9%; Pred. No. 0;
Matches 149; Conservative 1; Mismatches 7; Indels 0; Gaps 0;

Qy      1 VRSSRTSPDMPVHVHVANPQAEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
Db      1 VRSSRTSPDMPVHVHVANPQAEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
Qy      61 QVLFXGQGCSTHLLTHITISRIASVYQTXVNLLSAIXSPCQRETPEGAXPMYEPYIL 120
Db      61 QVLFSGQGCSTHLLTHITISRIASVYQTPVNLLSAIRSPCQRETPEGAXPMYEPYIL 120
Qy      121 GGVFQLEKGDRLSAEINRPDYLDPAESGQVYFGIIAL 157
Db      121 GGVFQLEKGDRLSAEINRPDYLDPAESGQVYFGIIAL 157

RESULT 3
AEB45432
ID      AEB45432 standard; protein; 157 AA.
XX
AC      AEB45432;
XX
DT      22-SEP-2005 (first entry)
XX
DE      TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:16.
XX
KW      tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW      autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW      acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW      plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
KW      antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW      antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW      vasotropic; cerebroprotective; dermatological; immunomodulator;
KW      antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW      mutein.
XX
OS      Homo sapiens.
OS      Synthetic.
XX
PN      WO2005066206-A1.
XX
PD      21-JUL-2005.
XX
PF      05-JAN-2005; 2005WO-JP0000032.
XX
PR      06-JAN-2004; 2004JP-00001427.
XX
PA      (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA      (MAYU)/ MAYUMI T.
PA      (TSUT)/ TSUTSUMI Y.
PA      (NAKA)/ NAKAGAWA S.
XX
PI      Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
DR      WPI; 2005-506850/51.
XX      N-PSDB; AEB45446.
XX
PT      Novel tumor necrosis factor TNF mutant protein, useful for treating
PT      and/or preventing diseases such as inflammation, and other diseases
PT      caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT      rheumatoid arthritis, allergy.

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XX PS Claim 4; SEQ ID NO 16; 34bp; Japanese.
XX PR
XX PA The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX PA particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX PA TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX PA a TNF mutant protein comprising an amino acid sequence derived from the
XX PA human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX PA one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX PA N-terminus, and amino acid residues at positions 84-89 by other amino
XX PA acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX PA mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX PA protein. The TNF mutant proteins are useful for treating and/or
XX PA preventing diseases such as inflammation, and other diseases caused by
XX PA overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX PA cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX PA Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX PA transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX PA respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX PA lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX PA etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX PA represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
XX PA The sequence data for this patent did not form part of the printed
XX PA specification, but was obtained in electronic format directly from WIPO
XX PA at ftp.wipo.int/pub/published_pct_sequences.
XX SQ Sequence 157 AA;

Query Match 98.1%; Score 765; DB 1; Length 157;
Best Local Similarity 94.9%; Pred. No. 0;
Matches 149; Conservative 1; Mismatches 7; Indels 0; Gaps 0;

Qy 1 VRSSRTSPDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTSPDMPVAHVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFPGQCGPSTHLLTHTISRIAVSYQTQVNLISAIKSPCQRTPEGAEXPWYEPIYL 120
Db 61 QVLFPGQCGPSTHLLTHTISRIAVSYQTQVNLISAIKSPCQRTPEGAEXPWYEPIYL 120

Qy 121 GGVFQLEKXGDRLSAEINRPDYLDPFAGSQVYFGIALL 157
Db 121 GGVFQLEKXGDRLSAEINRPDYLDPFAGSQVYFGIALL 157

RESULT 4
AEB45434
ID AEB45434 standard; protein; 157 AA.
XX AC AEB45434;
XX DT 22-SEP-2005 (first entry)
XX DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:16.
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
XX KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
XX KW animalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX KW mutein.
XX OS Homo sapiens.
XX OS Synthetic.
XX PN WO200506206-A1.
XX PD 21-JUL-2005.
XX PF 05-JAN-2005; 2005WO-JP000032.

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XX PR 06-JAN-2004; 2004JP-00001427.
XX PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX PA (MAYU/) MAYUMI T.
XX PA (TSUT/) TSUTSUMI Y.
XX PA (NAKA/) NAKAGAWA S.
XX PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX DR WPI: 2005-506850/51.
XX DR N-PSDB; AEB45448.
XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
XX PT and/or preventing diseases such as inflammation, and other diseases
XX PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX PT rheumatoid arthritis, allergy.
XX PS Claim 4; SEQ ID NO 18; 34bp; Japanese.
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX CC a TNF mutant protein comprising an amino acid sequence derived from the
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX CC protein. The TNF mutant proteins are useful for treating and/or
XX CC preventing diseases such as inflammation, and other diseases caused by
XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
XX CC The sequence data for this patent did not form part of the printed
XX CC specification, but was obtained in electronic format directly from WIPO
XX CC at ftp.wipo.int/pub/published_pct_sequences.
XX SQ Sequence 157 AA;

Query Match 97.9%; Score 764; DB 1; Length 157;
Best Local Similarity 94.9%; Pred. No. 0;
Matches 149; Conservative 0; Mismatches 8; Indels 0; Gaps 0;

Qy 1 VRSSRTSPDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTSPDMPVAHVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFPGQCGPSTHLLTHTISRIAVSYQTQVNLISAIKSPCQRTPEGAEXPWYEPIYL 120
Db 61 QVLFPGQCGPSTHLLTHTISRIAVSYQTQVNLISAIKSPCQRTPEGAEXPWYEPIYL 120

Qy 121 GGVFQLEKXGDRLSAEINRPDYLDPFAGSQVYFGIALL 157
Db 121 GGVFQLEKXGDRLSAEINRPDYLDPFAGSQVYFGIALL 157

RESULT 5
AEB45430
ID AEB45430 standard; protein; 157 AA.
XX AC AEB45430;
XX DT 22-SEP-2005 (first entry)
XX DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:14..
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;

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KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
XX Homo sapiens.
OS Synthetic.
OS
XX
XX AEB45453;
PN WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
PI
XX
XX MPI; 2005-506850/51.
DR N-PSDB; AEB45444.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 4; SEQ ID NO 14; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
SQ
Query Match 97.7%; Score 762; DB 1; Length 157;
Best Local Similarity 94.3%; Pred. No. 0;
Matches 148; Conservative 2; Mismatches 7; Indels 0; Gaps 0;
QY 1 VRSSRTPSDXPVAVHVNPAEQQLQWLNRRALLANGVELNDQLVVPSEGLYLIIYS 60
DB 1 VRSSRTPSDMPVAVHVNPAEQQLQWLNRRALLANGVELNDQLVVPSEGLYLIIYS 60
QY 61 QVLFXGGCGCSTHLLTHTTISRIASVYQTXVNLISAIKSPCQRTPGCAXPWYEPYIL 120
DB 61 QVLFXGGCGCSTHLLTHTTISRIASVYQTPVNLISAIKSPCQRTPGCAXPWYEPYIL 120

QY 121 GGVFOLEXGDRLSAEINRPDYLDFAESGOVYFGIALL 157
DB 121 GGVFOLEXGDRLSAEINRPDYLDFAESGOVYFGIALL 157
RESULT 6
AEB45453 ID AEB45453 standard; protein; 157 AA.
XX
XX AEB45453;
DT 22-SEP-2005 (first entry)
XX
XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:37.
XX
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
XX Homo sapiens.
OS Synthetic.
OS
XX
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX MPI; 2005-506850/51.
DR N-PSDB; AEB45476.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 37; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:

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CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ Sequence 157 AA;

Query Match          97.3%; Score 759; DB 1; Length 157;
Best Local Similarity 94.9%; Pred. No. 0;
Matches 149; Conservative 0; Mismatches 8; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAHVAVNPAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVAVNPAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Qy 61 QVLFXGQGCPSHTVLLTHTTISRIVSVYQTVNLLSAIXSPCQRTPEGAEXPWEPIYL 120
Db 61 QVLFXGQGCPSHTVLLTHTTISRIVSVYQTVNLLSAIXSPCQRTPEGAEXPWEPIYL 120
Qy 121 GGVFQLEKXGDRLSAEINRNPVLDPAESGQVYFGIIAL 157
Db 121 GGVFQLEKXGDRLSAEINRNPVLDPAESGQVYFGIIAL 157

RESULT 7
AEB45431
ID AEB45431 standard; protein; 157 AA.
XX
AC AEB45431;
XX
DT 22-SEP-2005 (first entry)
XX
DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:15.
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipruritic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW muteln.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO2005066206-A1.
XX
PD 21-JUL-2005.
XX
PP 05-JAN-2005; 2005WO-JP000032.
XX
PR 06-JAN-2004; 2004JP-00001427.
XX
PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Teutsami Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
XX
DR N-PSDB; AEB45445.
XX
FT Novel tumor necrosis factor TNF mutant protein, useful for treating
FT and/or preventing diseases such as inflammation, and other diseases
FT caused by overexpression of TNF, such as autoimmune diseases, tumor,
FT rheumatoid arthritis, allergy.
XX
PS Claim 4; SEQ ID NO 15; 34pp; Japanese.
XX
CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or

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CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, cachexia,
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, AIDS, severe acute
CC transplant rejection, stroke, ischemia, retinosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ Sequence 157 AA;

Query Match          97.2%; Score 758; DB 1; Length 157;
Best Local Similarity 94.3%; Pred. No. 0;
Matches 148; Conservative 0; Mismatches 9; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAHVAVNPAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVAVNPAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Qy 61 QVLFXGQGCPSHTVLLTHTTISRIVSVYQTVNLLSAIXSPCQRTPEGAEXPWEPIYL 120
Db 61 QVLFXGQGCPSHTVLLTHTTISRIVSVYQTVNLLSAIXSPCQRTPEGAEXPWEPIYL 120
Qy 121 GGVFQLEKXGDRLSAEINRNPVLDPAESGQVYFGIIAL 157
Db 121 GGVFQLEKXGDRLSAEINRNPVLDPAESGQVYFGIIAL 157

RESULT 8
AEB45454
ID AEB45454 standard; protein; 157 AA.
XX
AC AEB45454;
XX
DT 22-SEP-2005 (first entry)
XX
DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:38.
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipruritic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW muteln.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO2005066206-A1.
XX
PD 21-JUL-2005.
XX
PP 05-JAN-2005; 2005WO-JP000032.
XX
PR 06-JAN-2004; 2004JP-00001427.
XX
PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.

```

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PA (TSUTU/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX MPI; 2005-506850/51.
XX N-PSDB; AEB45477.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 38; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
XX
XX Query Match 96.78; Score 754; DB 1; Length 157;
XX Best Local Similarity 94.38; Pred. No. 0;
XX Matches 146; Conservative 0; Mismatches 9; Indels 0; Gaps 0;
XX
Qy 1 VRSSRTPSDXPVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVAVNPQAEQQLQWNTGYANALLANGVELRDNLQVVPSEGLYLIYS 60
Qy 61 QVLFXGGGCPSTHLLTHTTISRIVSVQTVXNLLSAIXSPCQRTPEGAAXPWYEPIYL 120
Db 61 QVLFSGGGCPSTHLLTHTTISRIVSVQTPVXNLLSAIRSPCQRTPEGAANPWYEPIYL 120
Qy 121 GGVFQLEKXGDRLSAEINRPDYLDPAESGQVYFGIALL 157
Db 121 GGVFQLEKPGDRLSAEINRPDYLDPAESGQVYFGIALL 157
XX
XX RESULT 9
XX AEB45469
XX ID AEB45469 standard; protein; 157 AA.
XX
XX AC AEB45469;
XX
XX 22-SEP-2005 (first entry)
XX
XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:53.
XX
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;

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KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
XX Homo sapiens.
XX Synthetic.
XX
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX (MAYU/) MAYUMI T.
XX (TSUTU/) TSUTSUMI Y.
XX (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX MPI; 2005-506850/51.
XX N-PSDB; AEB45492.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 53; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
XX
XX Query Match 96.4%; Score 752; DB 1; Length 157;
XX Best Local Similarity 93.6%; Pred. No. 0;
XX Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;
XX
Qy 1 VRSSRTPSDXPVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
Qy 61 QVLFXGGGCPSTHLLTHTTISRIVSVQTVXNLLSAIXSPCQRTPEGAAXPWYEPIYL 120
Db 61 QVLFSGGGCPSTHLLTHTTISRITKSYKPVNLLSAIRSPCQRTPEGAANPWYEPIYL 120
Qy 121 GGVFQLEKXGDRLSAEINRPDYLDPAESGQVYFGIALL 157
Db 121 GGVFQLEKPGDRLSAEINRPDYLDPAESGQVYFGIALL 157

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OS Synthetic.
XX WO2005066206-A1.
XX 21-JUL-2005.
XX 05-JAN-2005; 2005WO-JP000032.
XX 06-JAN-2004; 2004JP-00001427.
XX (HAYB ) HAYASHIBARA SEITBUTSU KAGAKU.
XX (MAYU/) MAYUMI T.
XX (TSUT/) TSUTSUMI Y.
XX (NAKA/) NAKAGAWA S.
XX Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45483.
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX Claim 5; SEQ ID NO 44; 34pp; Japanese.
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX Sequence 157 AA;
XX Query Match 96.2%; Score 750; DB 1; Length 157;
XX Best Local Similarity 93.0%; Pred. No. 0;
XX Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;
Qy 1 VRSSRTPSDXPVAHVANPQAEQOLWLNRRALLANGVELRDNLQVPSGGLYLYS 60
Db 1 VRSSRTPSDMPVAHVANPQAEQOLWLNRRALLANGVELRDNLQVPSGGLYLYS 60
Qy 61 QVLFKGGCGPSTHLLTHTTISRIVSVQTXVNLLSAIXSPQRTPEGAEXPVVEPIYL 120
Db 61 QVLFSGGCGPSTHLLTHTTISRISVNYNGPVNLLSAIRSPQRTPEGAEXPVVEPIYL 120
Qy 121 GGVFQLEKGRDLRAEINRPDYLDPAESQGVYFGIAL 157
Db 121 GGVFQLEPGDLRAEINRPDYLDPAESQGVYFGIAL 157
XX RESULT 14
XX AEB45464
XX ID AEB45464 standard; protein; 157 AA.
XX

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AC AEB45464;
XX 22-SEP-2005 (first entry)
XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:48.
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimers disease;
XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX vasotropic; cerebroprotective; dermatological; immunomodulator;
XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX mitein.
XX Homo sapiens.
XX Synthetic.
XX WO2005066206-A1.
XX 21-JUL-2005.
XX 05-JAN-2005; 2005WO-JP000032.
XX 06-JAN-2004; 2004JP-00001427.
XX (HAYB ) HAYASHIBARA SEITBUTSU KAGAKU.
XX (MAYU/) MAYUMI T.
XX (TSUT/) TSUTSUMI Y.
XX (NAKA/) NAKAGAWA S.
XX Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45487.
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX Claim 5; SEQ ID NO 48; 34pp; Japanese.
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX Sequence 157 AA;
XX Query Match 96.2%; Score 750; DB 1; Length 157;
XX Best Local Similarity 93.0%; Pred. No. 0;
XX Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;
XX

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QY 1 VRSSRTSPDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLQVPSGLYLIYS 60
DB 1 VRSSRTSPDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLQVPSGLYLIYS 60
QY 61 QVLFPGGQCPSTHLLTHTRISIAVSQTXVNLLSAIXSPCQRETPEGARXPWYEPYIL 120
DB 61 QVLFPGGQCPSTHLLTHTRISIAVSQTXVNLLSAIXSPCQRETPEGARXPWYEPYIL 120
QY 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIIAL 157
DB 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIIAL 157

RESULT 15
AEB45472
ID AEB45472 standard; protein; 157 AA.
XX
AC AEB45472;
XX
DT 22-SEP-2005 (first entry)
XX
TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:56.
XX
tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimers disease;
XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX antipeptidic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX vasotropic; cerebroprotective; dermatological; immunomodulator;
XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX mutein.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO2005066206-A1.
XX
PD 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU//) MAYUMI T.
PA (TSUT//) TSUTSUMI Y.
PA (NAKA//) NAKAGAWA S.
XX
PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45495.
XX
PT Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 56; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon

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CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimers disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. NO. 0;
Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;

QY 1 VRSSRTSPDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLQVPSGLYLIYS 60
DB 1 VRSSRTSPDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLQVPSGLYLIYS 60
QY 61 QVLFPGGQCPSTHLLTHTRISIAVSQTXVNLLSAIXSPCQRETPEGARXPWYEPYIL 120
DB 61 QVLFPGGQCPSTHLLTHTRISIAVSQTXVNLLSAIXSPCQRETPEGARXPWYEPYIL 120
QY 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIIAL 157
DB 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIIAL 157

RESULT 16
AEB45471
ID AEB45471 standard; protein; 157 AA.
XX
AC AEB45471;
XX
DT 22-SEP-2005 (first entry)
XX
TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:55.
XX
tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimers disease;
XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX antipeptidic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX vasotropic; cerebroprotective; dermatological; immunomodulator;
XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX mutein.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO2005066206-A1.
XX
PD 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU//) MAYUMI T.
PA (TSUT//) TSUTSUMI Y.
PA (NAKA//) NAKAGAWA S.
XX
PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45494.
XX
PT Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases

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caused by overexpression of TNF, such as autoimmune diseases, tumor, rheumatoid arthritis, allergy.

Claim 5; SEQ ID NO 55; 34pp; Japanese.

The invention relates to tumor necrosis factor (TNF) mutant proteins, particularly tumor necrosis factor mutant proteins specific for TNF-R1 or TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses a TNF mutant protein comprising an amino acid sequence derived from the human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the N-terminus, and amino acid residues at positions 84-89 by other amino acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF mutant protein; and (2) a TNF formulation comprising a TNF mutant protein. The TNF mutant proteins are useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumor, cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma), Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia, transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease, etc. The TNF mutant proteins are highly stable in vivo. This sequence represents a human TNF-alpha mutant protein specific for TNF-R2. Note: The sequence data for this patent did not form part of the printed specification, but was obtained in electronic format directly from WIPO at ftp.wipo.int/pub/published_pct_sequences.

Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRNALLANGVELDNLQVWPESEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVANPQAEQQLWLNRRNALLANGVELDNLQVWPESEGLYLIYS 60
Qy 61 QVLFPGQGPCSTHLLTHITISRIAVSYQTQVNLSSAIXSPCQRETPEGAEXPWVEPIYL 120
Db 61 QVLFSGQGPCSTHLLTHITISRIITPGVPSVNLSSAIXSPCQRETPEGAEXPWVEPIYL 120
Qy 121 GGVPQLEXGDRLSAEINRPDYLDPAESGQVYFGIIAL 157
Db 121 GGVPQLEPGDRLSAEINRPDYLDPAESGQVYFGIIAL 157

RESULT 17
AEB45455
.ID AEB45455 standard; protein; 157 AA.

XX AEB45455;
AC AEB45455;
XX 22-SEP-2005 (first entry)
DT TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:39.
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antiporiatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW muten.

OS Homo sapiens.
OS Synthetic.
XX WO200506206-A1.
XX 21-JUL-2005.

05-JAN-2005; 2005WO-JP000032.
06-JAN-2004; 2004JP-00001427.
(HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
(MAYU/) MAYUMI T.
(TSUT/) TSUTSUMI Y.
(NAKA/) NAKAGAWA S.
Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
WPI; 2005-506850/51.
N-PSDB; AEB45478.
Novel tumor necrosis factor TNF mutant protein, useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumor, rheumatoid arthritis, allergy.

Claim 5; SEQ ID NO 39; 34pp; Japanese.

The invention relates to tumor necrosis factor (TNF) mutant proteins, particularly tumor necrosis factor mutant proteins specific for TNF-R1 or TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses a TNF mutant protein comprising an amino acid sequence derived from the human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the N-terminus, and amino acid residues at positions 84-89 by other amino acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF mutant protein; and (2) a TNF formulation comprising a TNF mutant protein. The TNF mutant proteins are useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma), Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia, transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease, etc. The TNF mutant proteins are highly stable in vivo. This sequence represents a human TNF-alpha mutant protein specific for TNF-R2. Note: The sequence data for this patent did not form part of the printed specification, but was obtained in electronic format directly from WIPO at ftp.wipo.int/pub/published_pct_sequences.

Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
Best Local Similarity 93.6%; Pred. No. 0;
Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRNALLANGVELDNLQVWPESEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVANPQAEQQLWLNRRNALLANGVELDNLQVWPESEGLYLIYS 60
Qy 61 QVLFPGQGPCSTHLLTHITISRIAVSYQTQVNLSSAIXSPCQRETPEGAEXPWVEPIYL 120
Db 61 QVLFSGQGPCSTHLLTHITISRIAVSYQTQVNLSSAIXSPCQRETPEGAEXPWVEPIYL 120
Qy 121 GGVPQLEXGDRLSAEINRPDYLDPAESGQVYFGIIAL 157
Db 121 GGVPQLEPGDRLSAEINRPDYLDPAESGQVYFGIIAL 157

RESULT 18
AEB45466
.ID AEB45466 standard; protein; 157 AA.
XX AEB45466;
AC AEB45466;
XX 22-SEP-2005 (first entry)
DT TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:50.
XX

```

XX  tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW  autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW  acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW  plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW  antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW  antipeoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW  vasotropic; cerebroprotective; dermatological; immunomodulator;
KW  antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW  mtein.
XX
XX  Homo sapiens.
OS
OS  Synthetic.
XX
XX  WO2005066206-A1.
PN
XX
XX  21-JUL-2005.
PD
XX
XX  05-JAN-2005; 2005WO-JP000032.
PF
XX
XX  06-JAN-2004; 2004JP-00001427.
PR
XX
XX  (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA
XX  (MAYU/) MAYUMI T.
PA  (TSUT/) TSUTSUMI Y.
PA  (NAKA/) NAKAGAWA S.
XX
XX  Mayumi T, Teatsumi Y, Nakagawa S, Ohta T;
PI
XX  WPI; 2005-506850/51.
XX  N-PSDB; AEB45489.
DR
XX
XX  Novel tumor necrosis factor TNF mutant protein, useful for treating
PT  and/or preventing diseases such as inflammation, and other diseases
PT  caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT  rheumatoid arthritis, allergy.
XX
XX  Claim 5; SEQ ID NO 50; 34pp; Japanese.
PS
XX
XX  The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC  particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC  TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC  a TNF mutant protein comprising an amino acid sequence derived from the
CC  human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC  one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC  N-terminus, and amino acid residues at positions 84-89 by other amino
CC  acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC  mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC  protein. The TNF mutant proteins are useful for treating and/or
CC  preventing diseases such as inflammation, and other diseases caused by
CC  overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC  cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC  Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC  transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC  respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC  lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC  etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC  represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC  The sequence data for this patent did not form part of the printed
CC  specification, but was obtained in electronic format directly from WIPO
CC  at ftp.wipo.int/pub/published_pct_sequences.
XX
XX  Sequence 157 AA;
SQ
Query Match
Best Local Similarity 96.0%; Score 749; DB 1; Length 157;
Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;

QY  1 VRSSRTPSDXPAHVAVNVAQEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
Db  1 VRSSRTPSDMPVAHVAVNVAQEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
QY  61 QVLFSGGCGPSTHVLTHTTISRISKYTHSPVNLSSAIRSPCQRETPEGAENPWYEPYIL 120
Db  61 QVLFSGGCGPSTHVLTHTTISRISKYTHSPVNLSSAIRSPCQRETPEGAENPWYEPYIL 120
QY  121 GGVFQLEXGDRLSAEINRPDYLDFASSGQVYFGIIAL 157
Db  121 GGVFQLEPGDRLSAEINRPDYLDFASSGQVYFGIIAL 157

RESULT 19
AEB45474
ID  AEB45474 standard; protein; 157 AA.
XX
XX  AEB45474;
AC
XX
XX  22-SEP-2005 (first entry)
DT
XX
XX  TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:58.
DE
XX
XX  tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW  autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW  acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW  plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW  antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW  antipeoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW  vasotropic; cerebroprotective; dermatological; immunomodulator;
KW  antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW  mtein.
XX
XX  Homo sapiens.
OS
OS  Synthetic.
XX
XX  WO2005066206-A1.
PN
XX
XX  21-JUL-2005.
PD
XX
XX  05-JAN-2005; 2005WO-JP000032.
PF
XX
XX  06-JAN-2004; 2004JP-00001427.
PR
XX
XX  (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA
XX  (MAYU/) MAYUMI T.
PA  (TSUT/) TSUTSUMI Y.
PA  (NAKA/) NAKAGAWA S.
XX
XX  Mayumi T, Teatsumi Y, Nakagawa S, Ohta T;
PI
XX  WPI; 2005-506850/51.
XX  N-PSDB; AEB45497.
DR
XX
XX  Novel tumor necrosis factor TNF mutant protein, useful for treating
PT  and/or preventing diseases such as inflammation, and other diseases
PT  caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT  rheumatoid arthritis, allergy.
XX
XX  Claim 5; SEQ ID NO 58; 34pp; Japanese.
PS
XX
XX  The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC  particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC  TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC  a TNF mutant protein comprising an amino acid sequence derived from the
CC  human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC  one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC  N-terminus, and amino acid residues at positions 84-89 by other amino
CC  acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC  mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC  protein. The TNF mutant proteins are useful for treating and/or
CC  preventing diseases such as inflammation, and other diseases caused by
CC  overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC  cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC  Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC  transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC  respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC  lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC  etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC  represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC  The sequence data for this patent did not form part of the printed
CC  specification, but was obtained in electronic format directly from WIPO
CC  at ftp.wipo.int/pub/published_pct_sequences.
XX
XX  Sequence 157 AA;
SQ
Query Match
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;

QY  1 VRSSRTPSDXPAHVAVNVAQEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
Db  1 VRSSRTPSDMPVAHVAVNVAQEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
QY  61 QVLFSGGCGPSTHVLTHTTISRISKYTHSPVNLSSAIRSPCQRETPEGAENPWYEPYIL 120

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CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
 Best Local Similarity 93.6%; Pred. No. 0;
 Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAHVAVNPQAEQOLWLNRRANALLANGVELRDNLVWPSEGGLYLIYS 60
 Db 1 VRSSRTPSDMPVAHVAVNPQAEQOLWLNRRANALLANGVELRDNLVWPSEGGLYLIYS 60
 Qy 61 QVLFPGGCGCPSTHLLTHTTSRIASVQTXVNLISAIKSPCQRTPEGAEXPVEPIYL 120
 Db 61 QVLFPGGCGCPSTHLLTHTTSRIASVQTXVNLISAIKSPCQRTPEGAEXPVEPIYL 120
 Qy 121 GGVFQLEPGDRLSAEINRPNLDPAESGQVYFGIIAL 157
 Db 121 GGVFQLEPGDRLSAEINRPNLDPAESGQVYFGIIAL 157

RESULT 20
 AEB45475
 ID AEB45475 standard; protein; 157 AA.
 AC AEB45475;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:41.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antiporiatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.
 OS Homo sapiens.
 OS Synthetic.
 XX
 FN WO200506206-A1.
 XX
 PD 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 PF
 PR 06-JAN-2004; 2004JP-00001427.
 PR
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 XX Mayumi T, Teutsuni Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 DR N-PSDB; AEB45480.
 DR
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 XX Claim 5; SEQ ID NO 41; 34pp; Japanese.
 PS
 XX

CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, retinosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAHVAVNPQAEQOLWLNRRANALLANGVELRDNLVWPSEGGLYLIYS 60
 Db 1 VRSSRTPSDMPVAHVAVNPQAEQOLWLNRRANALLANGVELRDNLVWPSEGGLYLIYS 60
 Qy 61 QVLFPGGCGCPSTHLLTHTTSRIASVQTXVNLISAIKSPCQRTPEGAEXPVEPIYL 120
 Db 61 QVLFPGGCGCPSTHLLTHTTSRIASVQTXVNLISAIKSPCQRTPEGAEXPVEPIYL 120
 Qy 121 GGVFQLEPGDRLSAEINRPNLDPAESGQVYFGIIAL 157
 Db 121 GGVFQLEPGDRLSAEINRPNLDPAESGQVYFGIIAL 157

RESULT 21
 AEB45475
 ID AEB45475 standard; protein; 157 AA.
 XX
 AC AEB45475;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:59.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antiporiatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.
 OS Homo sapiens.
 OS Synthetic.
 XX
 FN WO200506206-A1.
 XX
 PD 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 PF
 PR 06-JAN-2004; 2004JP-00001427.
 PR

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PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX
PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45498.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 59; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, cachexia,
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPKVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60

Qy 61 QVLFXGGGCPSTHLLTHTTISRIVASYQTXXVNLLSAIXSPCQRETPGGAAXPWYEPIYL 120
Db 61 QVLFSGGCGPSTHLLTHTTISRISADYPHPVNLLSAIRSPCQRETPGGAANPWYEPIYL 120

Qy 121 GGVPQLXGDRLSAENRDPYLDPAESGGVYFGIALL 157
Db 121 GGVPQLXGDRLSAENRDPYLDPAESGGVYFGIALL 157

RESULT 22
AEB45458
ID AEB45458 standard; protein; 157 AA.
XX
XX AEB45458;
XX
XX 22-SEP-2005 (first entry)
XX
XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:42.
XX
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;

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KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
XX Homo sapiens.
OS Synthetic.
XX
XX WO2005066206-A1.
PN
XX 21-JUL-2005.
PD
XX 05-JAN-2005; 2005WO-JP000032.
PF
XX 06-JAN-2004; 2004JP-00001427.
PR
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45481.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 42; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, cachexia,
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;

Query Match 95.9%; Score 748; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPKVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60

Qy 61 QVLFXGGGCPSTHLLTHTTISRIVASYQTXXVNLLSAIXSPCQRETPGGAAXPWYEPIYL 120
Db 61 QVLFSGGCGPSTHLLTHTTISRISKTYPHPVNLLSAIRSPCQRETPGGAANPWYEPIYL 120

Qy 121 GGVPQLXGDRLSAENRDPYLDPAESGGVYFGIALL 157

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Db	121	GGVFQLEPGDRLSAEINRPDYLDFAESGQVYFGIIAL	157
RESULT 23			
AEBA5473			
ID	AEBA5473	standard; protein; 157 AA.	
XX	AC	AEBA5473;	
XX	DT	22-SEP-2005 (first entry)	
XX	DE	TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:57.	
XX	KW	tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;	
XX	KW	autoimmune disease; tumor; transplant rejection; cardiovascular disease;	
XX	KW	acquired immune deficiency syndrome; severe acute respiratory syndrome;	
XX	KW	plasmadium infection; meningitis; hepatitis; Alzheimers disease;	
XX	KW	antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;	
XX	KW	antipsoptic; anti-HIV; antiarteriosclerotic; immunosuppressive;	
XX	KW	vasotropic; cerebroprotective; dermatological; immunomodulator;	
XX	KW	antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;	
XX	XX		
OS	OS	Homo sapiens.	
OS	OS	Synthetic.	
XX	XX	WO2005066206-A1.	
XX	XX	21-JUL-2005.	
XX	XX	05-JAN-2005; 2005WO-JP000032.	
XX	XX	06-JAN-2004; 2004JP-00001427.	
XX	PA	(HAYB) HAYASHIBARA SEIBUTSU KAGAKU.	
XX	PA	(MAYU)/ MAYUMI T.	
XX	PA	(TSUT)/ TSUTSUMI Y.	
XX	PA	(NAKA)/ NAKAGAWA S.	
XX	PI	Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;	
XX	DR	WPI; 2005-506850/51.	
XX	DR	N-PSDB; AEB45496.	
XX	PT	Novel tumor necrosis factor TNF mutant protein, useful for treating	
XX	PT	and/or preventing diseases such as inflammation, and other diseases	
XX	PT	caused by overexpression of TNF, such as autoimmune diseases, tumor,	
XX	PT	rheumatoid arthritis, allergy.	
XX	PS	Claim 5; SEQ ID NO 57; 34pp; Japanese.	
XX	CC	The invention relates to tumor necrosis factor (TNF) mutant proteins,	
XX	CC	particularly tumor necrosis factor mutant proteins specific for TNF-R1 or	
XX	CC	TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses	
XX	CC	a TNF mutant protein comprising an amino acid sequence derived from the	
XX	CC	human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of	
XX	CC	one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the	
XX	CC	N-terminus, and amino acid residues at positions 84-89 by other amino	
XX	CC	acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF	
XX	CC	mutant protein; and (2) a TNF formulation comprising a TNF mutant	
XX	CC	protein. The TNF mutant proteins are useful for treating and/or	
XX	CC	preventing diseases such as inflammation, and other diseases caused by	
XX	CC	overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon	
XX	CC	cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),	
XX	CC	Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,	
XX	CC	transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute	
XX	CC	respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic	
XX	CC	lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,	
XX	CC	etc. The TNF mutant proteins are highly stable in vivo. This sequence	
XX	CC	represents a human TNF-alpha mutant protein specific for TNF-R2. Note:	
XX	CC	The sequence data for this patent did not form part of the printed	
XX	CC	specification, but was obtained in electronic format directly from WIPO	
XX	CC	at ftp.wipo.int/pub/published_pct_sequences.	
XX	XX		
XX	SQ	Sequence 157. AA;	
XX	Query Match	95.9%; Score 748; DB 1; Length 157;	
XX	Best Local Similarity	93.0%; Pred. No. 0;	
XX	Matches 146; Conservative	1; Mismatches 10; Indels 0; Gaps 0;	
Qy	1	VRSSRTSPDXPAHVAVVANPQAEQQLWLNRRANALLANGVELRDNLVVPSEGLYLIYS	60
Db	1	VRSSRTSPDMPVAHVAVVANPQAEQQLWLNRRANALLANGVELRDNLVVPSEGLYLIYS	60
Qy	61	QVLEFGGCGCSTHVLTHTTISRIAVSVQTXVNLISAIYSPCQRETPGCAEAXPWVEPIYL	120
Db	61	QVLEFGGCGCSTHVLTHTTISRIATYSSPVNLLSAIRSPCQRETPGCAEAXPWVEPIYL	120
Qy	121	GGVFQLEPGDRLSAEINRPDYLDFAESGQVYFGIIAL	157
Db	121	GGVFQLEPGDRLSAEINRPDYLDFAESGQVYFGIIAL	157
RESULT 24			
AEBA5467			
ID	AEBA5467	standard; protein; 157 AA.	
XX	AC	AEBA5467;	
XX	DT	22-SEP-2005 (first entry)	
XX	DE	TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:51.	
XX	KW	tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;	
XX	KW	autoimmune disease; tumor; transplant rejection; cardiovascular disease;	
XX	KW	acquired immune deficiency syndrome; severe acute respiratory syndrome;	
XX	KW	plasmadium infection; meningitis; hepatitis; Alzheimers disease;	
XX	KW	antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;	
XX	KW	antipsoptic; anti-HIV; antiarteriosclerotic; immunosuppressive;	
XX	KW	vasotropic; cerebroprotective; dermatological; immunomodulator;	
XX	KW	antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;	
XX	XX		
OS	OS	Homo sapiens.	
OS	OS	Synthetic.	
XX	XX	WO2005066206-A1.	
XX	XX	21-JUL-2005.	
XX	XX	05-JAN-2005; 2005WO-JP000032.	
XX	XX	06-JAN-2004; 2004JP-00001427.	
XX	PA	(HAYB) HAYASHIBARA SEIBUTSU KAGAKU.	
XX	PA	(MAYU)/ MAYUMI T.	
XX	PA	(TSUT)/ TSUTSUMI Y.	
XX	PA	(NAKA)/ NAKAGAWA S.	
XX	PI	Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;	
XX	DR	WPI; 2005-506850/51.	
XX	DR	N-PSDB; AEB45496.	
XX	PT	Novel tumor necrosis factor TNF mutant protein, useful for treating	
XX	PT	and/or preventing diseases such as inflammation, and other diseases	
XX	PT	caused by overexpression of TNF, such as autoimmune diseases, tumor,	
XX	PT	rheumatoid arthritis, allergy.	
XX	PS	Claim 5; SEQ ID NO 51; 34pp; Japanese.	
XX	CC	The invention relates to tumor necrosis factor (TNF) mutant proteins,	
XX	CC	particularly tumor necrosis factor mutant proteins specific for TNF-R1 or	
XX	CC	TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses	
XX	CC	a TNF mutant protein comprising an amino acid sequence derived from the	
XX	CC	human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of	
XX	CC	one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the	
XX	CC	N-terminus, and amino acid residues at positions 84-89 by other amino	
XX	CC	acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF	
XX	CC	mutant protein; and (2) a TNF formulation comprising a TNF mutant	
XX	CC	protein. The TNF mutant proteins are useful for treating and/or	
XX	CC	preventing diseases such as inflammation, and other diseases caused by	
XX	CC	overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon	
XX	CC	cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),	
XX	CC	Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,	
XX	CC	transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute	
XX	CC	respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic	
XX	CC	lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,	
XX	CC	etc. The TNF mutant proteins are highly stable in vivo. This sequence	
XX	CC	represents a human TNF-alpha mutant protein specific for TNF-R2. Note:	
XX	CC	The sequence data for this patent did not form part of the printed	
XX	CC	specification, but was obtained in electronic format directly from WIPO	
XX	CC	at ftp.wipo.int/pub/published_pct_sequences.	

XX	Homo sapiens.
OS	Synthetic.
XX	
XX	WO2005066206-A1.
XX	
XX	21-JUL-2005.
PD	
XX	
XX	05-JAN-2005; 2005WO-JP000032.
XX	
XX	06-JAN-2004; 2004JP-00001427.
XX	
XX	(HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
PA	(MAYU/) MAYUMI T.
PA	(TSUT/) TSUTSUMI Y.
PA	(NAKA/) NAKAGAWA S.
XX	
PI	Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX	
DR	WPI; 2005-506850/51.
DR	N-PSDB; AEB45451.
XX	
PT	Novel tumor necrosis factor TNF mutant protein, useful for treating
PT	and/or preventing diseases such as inflammation, and other diseases
PT	caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT	rheumatoid arthritis, allergy.
XX	
PS	Claim 4; SEQ ID NO 21; 34pp; Japanese.
XX	
CC	The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC	particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC	TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC	a TNF mutant protein comprising an amino acid sequence derived from the
CC	human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC	one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC	N-terminus, and amino acid residues at positions 84-89 by other amino acid
CC	acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC	mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC	protein. The TNF mutant proteins are useful for treating and/or
CC	preventing diseases such as inflammation, and other diseases caused by
CC	overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC	cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC	Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC	transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC	respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC	lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC	etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC	represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
CC	The sequence data for this patent did not form part of the printed
CC	specification, but was obtained in electronic format directly from WIPO
CC	at ftp.wipo.int/pub/published_pct_sequences.
XX	
SQ	Sequence 157 AA;
	Query Match 95.8%; Score 747; DB 1; Length 157;
	Best Local Similarity 92.4%; Pred. No. 0;
	Matches 145; Conservative 3; Mismatches 9; Indels 0; Gaps 0
Qy	1 VRSSRTPSDXPVAVHVANPQAEGLQWLNRANALLANGVELRNQLVVPSEGLYLYIS 60
Dd	1 VRSSRTPSDMPVAVHVANPQAEGLQWLNRANALLANGVELRDNLVVPSEGLYLYIS 60
Qy	61 QVLFXGQCPCSTHLLTHTTISRIVSYQTYNLISAIXPCORETPEGAEXPWEPIYL 120
Dd	61 QVLFSGQCPCSTHLLTHTTISRISTHNQPNVLSAIRSPCORETPEGAEXPWEPIYL 120
Qy	121 GGVFQLEKGDRLSAEINRPDYLDFAESGVFGIIAL 157
Dd	121 GGVFQLEPGDRLSAEINRPDYLDFAESGVFGIIAL 157
RESULT 27	
AEB45462	

Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

QY 1 VRSSRTSPDXPVAVHVNPAEQQLWLNRRNALLANGVELRDNLQVVPSEGLYLYS 60
 |||||
 Db 1 VRSSRTSPDXPVAVHVNPAEQQLWLNRRNALLANGVELRDNLQVVPSEGLYLYS 60
 |||||

QY 61 QVLFQXGQCPSTHLLTHTISRTAVSYQTKVNLLSAIXSPCORETPEGAEAXPWYEPYIL 120
 |||||
 Db 61 QVLFQXGQCPSTHLLTHTISRTAVSYQTKVNLLSAIXSPCORETPEGAEAXPWYEPYIL 120
 |||||

QY 121 GGVFQLEPGDRLSABEINRDPDLPFAESGQVYFGIIAL 157
 |||||
 Db 121 GGVFQLEPGDRLSABEINRDPDLPFAESGQVYFGIIAL 157
 |||||

RESULT 28
 AEB45470
 ID AEB45470 standard; protein; 157 AA.

XX AEB45470;
 AC
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:54.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipeoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.

XX Homo sapiens.
 OS Synthetic.
 OS
 PN WO2005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 PF 05-JAN-2005; 2005WO-JP000032.
 XX
 PR 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.

XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 PI
 XX WPI; 2005-506850/51.
 DR N-PSDB; AEB45493.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 PS Claim 5; SEQ ID NO 54; 34pp; Japanese.

XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or

CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX Sequence 157 AA;

Query Match 95.8%; Score 747; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 0; Mismatches 11; Indels 0; Gaps 0;

QY 1 VRSSRTSPDXPVAVHVNPAEQQLWLNRRNALLANGVELRDNLQVVPSEGLYLYS 60
 |||||
 Db 1 VRSSRTSPDXPVAVHVNPAEQQLWLNRRNALLANGVELRDNLQVVPSEGLYLYS 60
 |||||

QY 61 QVLFQXGQCPSTHLLTHTISRTAVSYQTKVNLLSAIXSPCORETPEGAEAXPWYEPYIL 120
 |||||
 Db 61 QVLFQXGQCPSTHLLTHTISRTAVSYQTKVNLLSAIXSPCORETPEGAEAXPWYEPYIL 120
 |||||

QY 121 GGVFQLEPGDRLSABEINRDPDLPFAESGQVYFGIIAL 157
 |||||
 Db 121 GGVFQLEPGDRLSABEINRDPDLPFAESGQVYFGIIAL 157
 |||||

RESULT 29
 AEB45456
 ID AEB45456 standard; protein; 157 AA.

XX AEB45456;
 AC
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:40.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipeoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.

XX Homo sapiens.
 OS Synthetic.
 OS
 PN WO2005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 PF 05-JAN-2005; 2005WO-JP000032.
 XX
 PR 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.

XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 PI
 XX WPI; 2005-506850/51.
 DR N-PSDB; AEB45479.

PT Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.

PS Claim 5; SEQ ID NO 40; 34pp; Japanese.

XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 95.6%; Score 746; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;
 Qy 1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLQVWVSEGLYLIYS 60
 Db 1 VRSSRTPSDMPVAHVANPQAEQQLWKNAGANALLANGVELRDNLQVWVSEGLYLIYS 60
 Qy 61 QVLFQGXGDRLSAEINRPNVLTISRIAVSYQTVNLLSAIXSPCQRETPEGAEXPWYEPYIL 120
 Db 61 QVLFSGQGCPSPTHVLLTHTISRIVSYQTVNLLSAIXSPCQRETPEGAEXPWYEPYIL 120
 Qy 121 GGVFQLEKXGDRLSAEINRPNVLTISRIAVSYQTVNLLSAIXSPCQRETPEGAEXPWYEPYIL 157
 Db 121 GGVFQLEKXGDRLSAEINRPNVLTISRIAVSYQTVNLLSAIXSPCQRETPEGAEXPWYEPYIL 157

RESULT 30

AEBA45459

ID AEB45459 standard; protein; 157 AA.

XX AC AEB45459;

XX DT 22-SEP-2005 (first entry)

XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:43.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmadium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritis; antiallergic;
 KW antipapillary; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW muten.

XX Homo sapiens.

OS Synthetic.

XX WO2005066206-A1.

XX 21-JUL-2005.
 XX 05-JAN-2005; 2005WO-JP0000032.
 XX 06-JAN-2004; 2004JP-00001427.
 PA (HAYB.) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 XX (NAKA/) NAKAGAWA S.

PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 DR N-PSDB; AEB45482.

XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.

PS Claim 5; SEQ ID NO 43; 34pp; Japanese.

XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 95.6%; Score 746; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;
 Qy 1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLQVWVSEGLYLIYS 60
 Db 1 VRSSRTPSDMPVAHVANPQAEQQLWLNRRNALLANGVELRDNLQVWVSEGLYLIYS 60
 Qy 61 QVLFQGXGDRLSAEINRPNVLTISRIAVSYQTVNLLSAIXSPCQRETPEGAEXPWYEPYIL 120
 Db 61 QVLFSGQGCPSPTHVLLTHTISRIVSYQTVNLLSAIXSPCQRETPEGAEXPWYEPYIL 120
 Qy 121 GGVFQLEKXGDRLSAEINRPNVLTISRIAVSYQTVNLLSAIXSPCQRETPEGAEXPWYEPYIL 157
 Db 121 GGVFQLEKXGDRLSAEINRPNVLTISRIAVSYQTVNLLSAIXSPCQRETPEGAEXPWYEPYIL 157

RESULT 31

AEBA45465

ID AEB45465 standard; protein; 157 AA.

XX AC AEB45465;

XX DT 22-SEP-2005 (first entry)

```

XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:49.
XX
XX
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimers disease;
XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX antipeptic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX vasotropic; cerebroprotective; dermatological; immunomodulator;
XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX mutin.
XX
XX Homo sapiens.
XX Synthetic.
XX
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX (MAYU/) MAYUMI T.
XX (TSUT/) TSUTSUMI Y.
XX (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX NPI; 2005-506850/51.
XX N-PSDB; AEB45488.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 49; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins.
XX Particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
XX
XX Query Match 95.6%; Score 746; DB 1; Length 157;
XX Best Local Similarity 93.0%; Pred. No. 0;
XX Matches 146; Conservative 0; Mismatches 11; Indels 0; Gaps 0;
XX
XX 1 VRSSRRTPSDXPVAHVAVNPAEQQLQWLNRRANALLANGVELRDNLQVVPSEGLYLIYS 60
XX
XX 1 VRSSRRTPSDMPVAHVAVNPAEQQLQWLNRRANALLANGVELRDNLQVVPSEGLYLIYS 60
XX

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```

QY 61 QVLFQGGCPSTHVLTLTHTTISRIVSYQTXVNLLSAIXSPCQRETPGGAENPWEPIYL 120
DB 61 QVLFQGGCPSTHVLTLTHTTISRITHKYPQVNLLSAIRSPCQRETPGGAENPWEPIYL 120
QY 121 GGVFQLEEXDRLSABENRDPYLDFAESGGVYFGIALL 157
DB 121 GGVFQLEPQDRLSABENRDPYLDFAESGGVYFGIALL 157
RESULT 32
AEB45463
ID AEB45463 standard; protein; 157 AA.
XX
XX AC AEB45463;
XX
XX 22-SEP-2005 (first entry)
XX
XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:47.
XX
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimers disease;
XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX vasotropic; cerebroprotective; dermatological; immunomodulator;
XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX mutin.
XX
XX Homo sapiens.
XX Synthetic.
XX
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX (MAYU/) MAYUMI T.
XX (TSUT/) TSUTSUMI Y.
XX (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45486.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 47; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute

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CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 95.6%; Score 746; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAHVAVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 Db 1 VRSSRTPSDMPVAHVAVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFKGGGCPSTHLLTHTTISRIVSVYQTWNLLSAIXSPCQRTTPGGAAXPWYEPYIL 120
 Db 61 QVLFSGGCGCPSTHLLTHTTISRIVSVYQTWNLLSAIXSPCQRTTPGGAAXPWYEPYIL 120

Qy 121 GGVFQLEPGDRLSAEINRNPDLDPFAESGQVYFGIIL 157
 Db 121 GGVFQLEPGDRLSAEINRNPDLDPFAESGQVYFGIIL 157

RESULT 33
 AEB45429
 ID AEB45429 standard; protein; 157 AA.

XX AC AEB45429;
 XX DT 22-SEP-2005 (first entry)
 XX DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:13.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmadium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antiporiatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.

XX OS Homo sapiens.
 XX OS Synthetic.
 XX PN WO2005066206-A1.
 XX PD 21-JUL-2005.

XX 05-JAN-2005; 2005WO-JP0000032.
 XX 06-JAN-2004; 2004JP-00001427.

XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.

XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 XX N-PSDB; AEB45443.

XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX

PS The invention relates to tumor necrosis factor (TNF) mutant proteins,
 XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 95.4%; Score 744; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 0; Mismatches 11; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAHVAVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 Db 1 VRSSRTPSDMPVAHVAVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFKGGGCPSTHLLTHTTISRIVSVYQTWNLLSAIXSPCQRTTPGGAAXPWYEPYIL 120
 Db 61 QVLFSGGCGCPSTHLLTHTTISRIVSVYQTWNLLSAIXSPCQRTTPGGAAXPWYEPYIL 120

Qy 121 GGVFQLEPGDRLSAEINRNPDLDPFAESGQVYFGIIL 157
 Db 121 GGVFQLEPGDRLSAEINRNPDLDPFAESGQVYFGIIL 157

RESULT 34

AEB45428
 ID AEB45428 standard; protein; 157 AA.

XX AC AEB45428;
 XX DT 22-SEP-2005 (first entry)
 XX DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:12.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmadium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antiporiatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.

XX OS Homo sapiens.

XX OS Synthetic.

XX PN WO2005066206-A1.

XX 21-JUL-2005.

XX 05-JAN-2005; 2005WO-JP0000032.

XX

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PR 06-JAN-2004; 2004JP-00001427.
XX
PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45442.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 4; SEQ ID NO 12; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ Sequence 157 AA;

Query Match 95.3%; Score 743; DB 1; Length 157;
Best Local Similarity 92.4%; Pred. No. 0;
Matches 145; Conservative 1; Mismatches 11; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLQWRNHSNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLPFGGCGCPSTHLLTHTTISRIVSVQTVNLLSAIXSPCQRTTPGAXPWEPIYL 120
Db 61 QVLPFGGCGCPSTHLLTHTTISRIVSVQTVNLLSAIXSPCQRTTPGAXPWEPIYL 120

Qy 121 GGVFQLBGRDLRSABINRPDYLDPAESQGVYFGIAL 157
Db 121 GGVFQLBGRDLRSABINRPDYLDPNAGVYFGIAL 157

RESULT 35
AEB45425
ID AEB45425 standard; protein; 157 AA.
XX
XX AEB45425;
XX
XX 22-SEP-2005 (first entry)
XX
XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:9.
DE tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX
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acquired immune deficiency syndrome; severe acute respiratory syndrome;
plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
antiinflammatory; cytostatic; antineoplastic; antithrombotic; antiallergic;
antipeptidic; anti-HIV; antiarteriosclerotic; immunosuppressive;
vasotropic; cerebroprotective; dermatological; immunomodulator;
antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
mucin.

Homo sapiens.
Synthetic.
WO2005066206-A1.
21-JUL-2005.
05-JAN-2005; 2005WO-JP000032.
06-JAN-2004; 2004JP-00001427.
(HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
(MAYU/) MAYUMI T.
(TSUT/) TSUTSUMI Y.
(NAKA/) NAKAGAWA S.
Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
WPI; 2005-506850/51.
N-PSDB; AEB45439.

Novel tumor necrosis factor TNF mutant protein, useful for treating
and/or preventing diseases such as inflammation, and other diseases
caused by overexpression of TNF, such as autoimmune diseases, tumor,
rheumatoid arthritis, allergy.

Claim 4; SEQ ID NO 9; 34pp; Japanese.

The invention relates to tumor necrosis factor (TNF) mutant proteins,
particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
a TNF mutant protein comprising an amino acid sequence derived from the
human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
N-terminus, and amino acid residues at positions 84-89 by other amino
acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
mutant protein; and (2) a TNF formulation comprising a TNF mutant
protein. The TNF mutant proteins are useful for treating and/or
preventing diseases such as inflammation, and other diseases caused by
overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
etc. The TNF mutant proteins are highly stable in vivo. This sequence
represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
The sequence data for this patent did not form part of the printed
specification, but was obtained in electronic format directly from WIPO
at ftp.wipo.int/pub/published_pct_sequences.

Sequence 157 AA;

Query Match 95.3%; Score 743; DB 1; Length 157;
Best Local Similarity 92.4%; Pred. No. 0;
Matches 145; Conservative 1; Mismatches 11; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLQWRNHSNALLANGVELRDNLVVPSEGLYLIYS 60
Qy 61 QVLPFGGCGCPSTHLLTHTTISRIVSVQTVNLLSAIXSPCQRTTPGAXPWEPIYL 120
Db 61 QVLPFGGCGCPSTHLLTHTTISRIVSVQTVNLLSAIXSPCQRTTPGAXPWEPIYL 120
Qy 121 GGVFQLBGRDLRSABINRPDYLDPAESQGVYFGIAL 157
Db 121 GGVFQLBGRDLRSABINRPDYLDPNAGVYFGIAL 157

RESULT 35
AEB45425
ID AEB45425 standard; protein; 157 AA.
XX
XX AEB45425;
XX
XX 22-SEP-2005 (first entry)
XX
XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:9.
DE tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX

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Qy 121 GGVFQLEGGDRLSAEINRPDYLDFAESGQVYFGIALL 157
    ||||| ||||| ||||| ||||| ||||| : ||||| |||||
Db 121 GGVFQLEGGDRLSAEINRPDYLDFAESGQVYFGIALL 157

RESULT 36
AEB45421
ID AEB45421 standard; protein; 157 AA.
XX
XX
AC AEB45421;
XX
XX
DT 22-SEP-2005 (first entry)
XX
DE 5 Human TNF-alpha mutant protein, SEQ ID No:5.
XX
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
XX
OS Homo sapiens.
OS Synthetic.
XX
XX
PN WO2005066206-A1.
XX
XX
PD 21-JUL-2005.
XX
XX
PF 05-JAN-2005; 2005WO-JP000032.
XX
XX
PR 06-JAN-2004; 2004JP-00001427.
XX
XX
PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU)/ MAYUMI T.
PA (TSUT)/ TSUTSUMI Y.
PA (NAKA)/ NAKAGAWA S.
XX
XX
PI Mayumi T, Teutsu Y, Nakagawa S, Ohta T;
XX
XX
WPI; 2005-506850/51.
DR N-PSDB; AEB45422.
XX
XX
PT Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX
PS Example 1; SEQ ID NO 5; 34pp; Japanese.
XX
XX
CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, sytemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents human TNF-alpha mutant protein. Note: The sequence data for
CC this patent did not form part of the printed specification, but was
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CC obtained in electronic format directly from WIPO at
CC ftp.wipo.int/pub/published_pct_sequences.
XX
XX
SQ Sequence 157 AA;
    Query Match 95.1%; Score 742; DB 1; Length 157;
    Best Local Similarity 92.4%; Pred. No. 0;
    Matches 145; Conservative 0; Mismatches 12; Indels 0; Gaps 0;
Qy 1 VRSSRTSPDXPAHVHVANPQAEQQLQWLNRRANALANGVELRDNLVVPSEGLYLIYS 60
    ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db 1 VRSSRTSPDXPAHVHVANPQAEQQLQWLNRRANALANGVELRDNLVVPSEGLYLIYS 60
Qy 61 QVLFQGGQCPSTHLLTHTISRIASVQTYVNLLSAIXSPCQRETPGAGANPWYEPIYL 120
    ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db 61 QVLFQGGQCPSTHLLTHTISRIASVQTYVNLLSAIXSPCQRETPGAGANPWYEPIYL 120
Qy 121 GGVFQLEGGDRLSAEINRPDYLDFAESGQVYFGIALL 157
    ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db 121 GGVFQLEGGDRLSAEINRPDYLDFAESGQVYFGIALL 157

RESULT 37
AEB45427
ID AEB45427 standard; protein; 157 AA.
XX
XX
AC AEB45427;
XX
XX
DT 22-SEP-2005 (first entry)
XX
XX
DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:11.
XX
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
XX
OS Homo sapiens.
OS Synthetic.
XX
XX
PN WO2005066206-A1.
XX
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PD 21-JUL-2005.
XX
XX
PF 05-JAN-2005; 2005WO-JP000032.
XX
XX
PR 06-JAN-2004; 2004JP-00001427.
XX
XX
PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU)/ MAYUMI T.
PA (TSUT)/ TSUTSUMI Y.
PA (NAKA)/ NAKAGAWA S.
XX
XX
PI Mayumi T, Teutsu Y, Nakagawa S, Ohta T;
XX
XX
WPI; 2005-506850/51.
DR N-PSDB; AEB45441.
XX
XX
PT Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX
PS Claim 4; SEQ ID NO 11; 34pp; Japanese.
XX
XX
CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
```

CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 95.0%; Score 741; DB 1; Length 157;
 Best Local Similarity 92.4%; Pred. No. 0;
 Matches 145; Conservative 1; Mismatches 11; Indels 0; Gaps 0;
 QY 1 VRSSRTPSDXPAHVAVNPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 DB 1 VRSSRTPSDMPVAHVAVNPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 QY 61 QVLFXGGCSTHLLTHTTISRIVSVQTVNLLSAIXSPCQRETPGAXPWYEPYIL 120
 DB 61 QVLFXGGCSTHLLTHTTISRIVSVQTVNLLSAIXSPCQRETPGAXPWYEPYIL 120
 QY 121 GGVFQLEPGDRLSAEINRPDYLDFAESGQVYFGIALL 157
 DB 121 GGVFQLEPGDRLSAEINRPDYLDFAESGQVYFGIALL 157

RESULT 38
 AEB45423
 ID AEB45423 standard; protein; 157 AA.
 XX
 AC AEB45423;
 XX
 DT 22-SEP-2005 (first entry)
 DE Human TNF-alpha mutant protein, SEQ ID No:7.
 XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW muten.

OS Homo sapiens.
 OS Synthetic.
 XX
 PN WO2005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 PF 05-JAN-2005; 2005WO-JP000032.
 XX
 PR 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.

(NAKA/) NAKAGAWA S.

Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;

WPI: 2005-506850/51.

N-PSDB; AEB45424.

Novel tumor necrosis factor TNF mutant protein, useful for treating
 and/or preventing diseases such as inflammation, and other diseases
 caused by overexpression of TNF, such as autoimmune diseases, tumor,
 rheumatoid arthritis, allergy.

Example 1; SEQ ID NO 7; 34pp; Japanese.

The invention relates to tumor necrosis factor (TNF) mutant proteins,
 particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 a TNF mutant protein comprising an amino acid sequence derived from the
 human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 N-terminus, and amino acid residues at positions 84-89 by other amino
 acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 mutant protein; and (2) a TNF formulation comprising a TNF mutant
 protein. The TNF mutant proteins are useful for treating and/or
 preventing diseases such as inflammation, and other diseases caused by
 overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 etc. The TNF mutant proteins are highly stable in vivo. This sequence
 represents human TNF-alpha mutant protein. Note: The sequence data for
 this patent did not form part of the printed specification, but was
 obtained in electronic format directly from WIPO at
 ftp.wipo.int/pub/published_pct_sequences.

Sequence 157 AA;

Query Match 95.0%; Score 741; DB 1; Length 157;
 Best Local Similarity 92.4%; Pred. No. 0;
 Matches 145; Conservative 0; Mismatches 12; Indels 0; Gaps 0;

QY 1 VRSSRTPSDXPAHVAVNPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

DB 1 VRSSRTPSDMPVAHVAVNPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

QY 61 QVLFXGGCSTHLLTHTTISRIVSVQTVNLLSAIXSPCQRETPGAXPWYEPYIL 120

DB 61 QVLFXGGCSTHLLTHTTISRIVSVQTVNLLSAIXSPCQRETPGAXPWYEPYIL 120

QY 121 GGVFQLEPGDRLSAEINRPDYLDFAESGQVYFGIALL 157

DB 121 GGVFQLEPGDRLSAEINRPDYLDFAESGQVYFGIALL 157

RESULT 39

AEB45435

ID AEB45435 standard; protein; 157 AA.

XX AEB45435;

XX 22-SEP-2005 (first entry)

XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:19.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;

XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;

XX acquired immune deficiency syndrome; severe acute respiratory syndrome;

XX plasmodium infection; meningitis; hepatitis; Alzheimer's disease;

XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;

XX antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;

XX vasotropic; cerebroprotective; dermatological; immunomodulator;


```
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mitein.
XX
OS Homo sapiens.
OS Synthetic.
XX
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP0000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX (MAYU/) MAYUMI T.
XX (TSUT/) TSUTSUMI Y.
XX (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45449.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 4; SEQ ID NO 19; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
XX
XX Query Match 95.0%; Score 741; DB 1; Length 157;
XX Best Local Similarity 92.4%; Pred. No. 0;
XX Matches 145; Conservative 1; Mismatches 11; Indels 0; Gaps 0;
XX
XX 1 VRSSRTSDXPFVAVHVNPAEQGLQWLNRRNALLANGVELRDNLQVLPSEGLYLIYS 60
XX
XX 1 VRSSRTSDXPFVAVHVNPAEQGLQWLNRRNALLANGVELRDNLQVLPSEGLYLIYS 60
XX
XX 61 QVLFVGQCPSTHLLTHTTISRIVSYQTXVNLISAIKSPQRETPGEAAXPWTEPIYL 120
XX
XX 61 QVLFVGQCPSTHLLTHTTISRITPAIRNPVNLISAIKSPQRETPGEAAXPWTEPIYL 120
XX
XX 121 GGVFQLEKXDRLSAENRPDYLDFAESGVVFGIIAL 157
XX
XX 121 GGVFQLEKXDRLSAENRPDYLDFAESGVVFGIIAL 157
```

```
RESULT 40
AEB45426
ID AEB45426 standard; protein; 146 AA.
XX
XX AEB45426;
AC
XX 22-SEP-2005 (first entry)
DT
XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:10.
DE
XX
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmoidium infection; meningitis; hepatitis; Alzheimer's disease;
KW antiinflammatory; cytostatic; antirheumatic; antithrombotic; antiallergic;
KW antipruritic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mitein.
XX
XX Homo sapiens.
OS Synthetic.
OS
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP0000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX (MAYU/) MAYUMI T.
XX (TSUT/) TSUTSUMI Y.
XX (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45440.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 4; SEQ ID NO 10; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 146 AA;
```

Query Match 89.5%; Score 698; DB 1; Length 146;
Best Local Similarity 93.8%; Pred. No. 0;
Matches 136; Conservative 1; Mismatches 8; Indels 0; Gaps 0;

Qy	1	VRSSRTPSDXPVAHVVANPQAEQQLQWLNRRANALLANGVELRDNQLVVPSEGLYLIYS	60
Db	1	VRSSRTPSDMPVAHVVANPQAEQQLQWLNRRANALLANGVELRDNQLVVPSEGLYLIYS	60
Qy	61	QVLFXGQGCPSHTVLLTHTTISRIVASYQTXXNLLSAIXSPCQRETPEGAEAXPWYEPIYL	120
Db	61	QVLFSGQGCPSHTVLLTHTTISRIVASYQTPVNLLSAIRSPCQRETPEGAEANPWYEPIYL	120
Qy	121	GGVFQLEXGDRLSAEINRPDYLDFA	145
Db	121	GGVFQLEPGDRLSAEINRPDYLDPS	145

Search completed: September 21, 2006, 14:40:08
Job time : 1 secs

GenCore version 5.1.9
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OM protein - protein search, using sw model

Run on: September 21, 2006, 09:09:19 ; Search time 0.001 Seconds
(without alignments)
1008.882 Million cell updates/sec

Title: US-10-668-178-2

Perfect score: 780

Sequence: 1 VRSSRTPTSDXPVAVHVPV.....RPDYLDFAESGVYFGIAL 157

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 41 seqs, 6426 residues

Total number of hits satisfying chosen parameters: 41

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 200 summaries

Database : xnotk.subdb.*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	774	99.2	157	ADH10159	Human tumour necro
2	773	99.1	157	ADH10160	Human tumour necro
3	766	98.2	157	ADH10160	TNF-R1 specific hu
4	765	98.1	157	ADH10160	TNF-R1 specific hu
5	764	97.9	157	ADH10160	TNF-R1 specific hu
6	762	97.7	157	ADH10160	TNF-R1 specific hu
7	759	97.3	157	ADH10160	TNF-R2 specific hu
8	758	97.2	157	ADH10160	TNF-R1 specific hu
9	754	96.7	157	ADH10160	TNF-R2 specific hu
10	752	96.4	157	ADH10160	TNF-R2 specific hu
11	751	96.3	157	ADH10160	TNF-R1 specific hu
12	751	96.3	157	ADH10160	TNF-R1 specific hu
13	751	96.3	157	ADH10160	TNF-R2 specific hu
14	750	96.2	157	ADH10160	TNF-R2 specific hu
15	750	96.2	157	ADH10160	TNF-R2 specific hu
16	749	96.0	157	ADH10160	TNF-R2 specific hu
17	749	96.0	157	ADH10160	TNF-R2 specific hu
18	749	96.0	157	ADH10160	TNF-R2 specific hu
19	749	96.0	157	ADH10160	TNF-R2 specific hu
20	749	96.0	157	ADH10160	TNF-R2 specific hu
21	749	96.0	157	ADH10160	TNF-R2 specific hu
22	749	96.0	157	ADH10160	TNF-R2 specific hu
23	748	95.9	157	ADH10160	TNF-R2 specific hu
24	748	95.9	157	ADH10160	TNF-R2 specific hu
25	748	95.9	157	ADH10160	TNF-R2 specific hu
26	748	95.9	157	ADH10160	TNF-R2 specific hu
27	747	95.8	157	ADH10160	TNF-R2 specific hu
28	747	95.8	157	ADH10160	TNF-R2 specific hu
29	747	95.8	157	ADH10160	TNF-R2 specific hu
30	746	95.6	157	ADH10160	TNF-R2 specific hu
31	746	95.6	157	ADH10160	TNF-R2 specific hu
32	746	95.6	157	ADH10160	TNF-R2 specific hu
33	746	95.6	157	ADH10160	TNF-R2 specific hu

34 744 95.4 157 1 AEB45429 TNF-R1 specific hu
35 743 95.3 157 1 AEB45428 TNF-R1 specific hu
36 743 95.3 157 1 AEB45425 TNF-R1 specific hu
37 742 95.1 157 1 AEB45421 Human TNF-alpha hu
38 741 95.0 157 1 AEB45427 TNF-R1 specific hu
39 741 95.0 157 1 AEB45423 Human TNF-alpha hu
40 741 95.0 157 1 AEB45435 TNF-R1 specific hu
41 698 89.5 146 1 AEB45426 TNF-R1 specific hu

ALIGNMENTS

RESULT 1
ADH10159
ID ADH10159 standard; protein; 157 AA.
XX
AC ADH10159;
XX
DT 11-MAR-2004 (first entry)
XX
DE Human tumour necrosis factor variant protein.
XX
KW TNF; tumour necrosis factor; polyethylene glycol; cytostatic; cancer;
KW human; variant.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Misc-difference 11
FT /label= Asp, Ala, Arg, Ser, Thr, Pro, Met or Leu
FT Misc-difference 65
FT /label= Asp, Ala, Arg, Ser, Thr, Pro, Met or Leu
FT Misc-difference 90
FT /label= Asp, Ala, Arg, Ser, Thr, Pro, Met or Leu
FT Misc-difference 98
FT /label= Asp, Ala, Arg, Ser, Thr, Pro, Met or Leu
FT Misc-difference 112
FT /label= Asp, Ala, Arg, Ser, Thr, Pro, Met or Leu
FT Misc-difference 128
FT /label= Asp, Ala, Arg, Ser, Thr, Pro, Met or Leu
XX
EPI354893-A2.
22-OCT-2003.
30-JAN-2003; 2003EP-00250587.
25-MAR-2002; 2002JP-00083509.
26-JUN-2002; 2002JP-00185387.
(HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
(MAYU/) MAYUMI T.
(TSUT/) TSUTSUMI Y.
(NAKA/) NAKAGAWA S.
Mayumi T, Tsutsumi Y, Nakagawa S, Ikegami H;
WPI; 2004-063952/07.

A physiologically active complex which comprises a protein part with tumor necrosis factor activity and a high molecular part has higher stability and retention in living bodies and is useful to treat disease, particularly cancer.

Claim 2; SEQ ID NO 2; 18pp; English.

The present sequence represents a physiologically active complex which comprises a proteinaceous part with tumour necrosis factor (TNF) activity and a high molecular part bound artificially to the N-terminus of the proteinaceous part. The proteinaceous part comprises the sequence selected from ADH10159 and the molecular part has a molecular weight of 500-5000 Da and is a homopolymer of polyethylene glycol or a copolymer of

CC ethylene glycol and its derivatives. The invention is used to treat
 CC susceptible disease, particularly cancer. The complex has a higher
 CC stability and longer retention time in living bodies than intact
 CC necrosis factor. The present sequence represents a human TNF variant
 CC protein.
 XX
 SQ Sequence 157 AA;

Query Match 99.2%; Score 774; DB 1; Length 157;
 Best Local Similarity 100.0%; Pred. No. 0;
 Matches 157; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 VRSSRTSPDXPVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLIYIS 60
 DB 1 VRSSRTSPDXPVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLIYIS 60
 QY 61 QVLPXGQGCPSHTVLLTHTTISRIVASYQTAVNLSAIXSPCQRETPEGAEAXPWYEPYIL 120
 DB 61 QVLPXGQGCPSHTVLLTHTTISRIVASYQTAVNLSAIXSPCQRETPEGAEAXPWYEPYIL 120
 QY 121 GGVPQLEXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157
 DB 121 GGVPQLEXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157

RESULT 2
 ADH10160
 ID ADH10160 standard; protein; 157 AA.
 AC ADH10160;
 XX
 DT 11-MAR-2004 (first entry)
 XX
 DE Human tumour necrosis factor variant protein.
 XX
 KW TNF; tumour necrosis factor; polyethylene glycol; cytostatic; cancer;
 KW human; variant.
 XX
 OS Homo sapiens.
 XX
 PN EPI354893-A2.
 XX
 PD 22-OCT-2003.
 XX
 PF 30-JAN-2003; 2003EP-00250587.
 XX
 PR 25-MAR-2002; 2002JP-00083509.
 PR 26-JUN-2002; 2002JP-00185387.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Teuteumi Y, Nakagawa S, Ikegami H;
 XX
 WPI; 2004-063952/07.
 DR N-PSDB; ADH10169.
 XX
 PT A physiologically active complex which comprises a protein part with
 PT tumor necrosis factor activity and a high molecular part has higher
 PT stability and retention in living bodies and is useful to treat disease,
 PT particularly cancer.
 XX
 PS Example 1; SEQ ID NO 3; 18pp; English.
 XX
 CC The present sequence represents a physiologically active complex which
 CC comprises a proteinaceous part with tumour necrosis factor (TNF) activity
 CC and a high molecular part bound artificially to the N-terminus of the
 CC proteinaceous part. The proteinaceous part comprises the sequence
 CC selected from ADH10159 and the molecular part has a molecular weight of
 CC 500-5000 Da and is a homopolymer of polyethylene glycol or a copolymer of
 CC ethylene glycol and its derivatives. The invention is used to treat

CC susceptible disease, particularly cancer. The complex has a higher
 CC stability and longer retention time in living bodies than intact tumour
 CC necrosis factor. The present sequence represents a human TNF variant
 CC protein.
 XX
 SQ Sequence 157 AA;

Query Match 99.1%; Score 773; DB 1; Length 157;
 Best Local Similarity 96.2%; Pred. No. 0;
 Matches 151; Conservative 0; Mismatches 6; Indels 0; Gaps 0;

QY 1 VRSSRTSPDXPVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLIYIS 60
 DB 1 VRSSRTSPDXPVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLIYIS 60
 QY 61 QVLPXGQGCPSHTVLLTHTTISRIVASYQTAVNLSAIXSPCQRETPEGAEAXPWYEPYIL 120
 DB 61 QVLPXGQGCPSHTVLLTHTTISRIVASYQTAVNLSAIXSPCQRETPEGAEAXPWYEPYIL 120
 QY 121 GGVPQLEXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157
 DB 121 GGVPQLEXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157

RESULT 3
 AEB45433
 ID AEB45433 standard; protein; 157 AA.
 AC AEB45433;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:17.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antiproliferative; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mucin.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 PN WO2005066206-A1.
 XX
 PD 21-JUL-2005.
 XX
 PF 05-JAN-2005; 2005WO-JP000032.
 XX
 PR 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Tsuteumi Y, Nakagawa S, Ohta T;
 XX
 WPI; 2005-506850/51.
 DR N-PSDB; AEB45447.
 XX
 PT Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 PS Claim 4; SEQ ID NO 17; 34pp; Japanese.
 XX
 CC The invention relates to tumor necrosis factor (TNF) mutant proteins,

particularly tumor necrosis factor mutant proteins specific for TNF-R1 or TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses a TNF mutant protein comprising an amino acid sequence derived from the human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the N-terminus, and amino acid residues at positions 84-89 by other amino acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF mutant protein. The TNF mutant proteins are useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumors, cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma), Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia, transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease, etc. The TNF mutant proteins are highly stable in vivo. This sequence represents a human TNF-alpha mutant protein specific for TNF-R1. Note: The sequence data for this patent did not form part of the printed specification, but was obtained in electronic format directly from WIPO at ftp.wipo.int/pub/published_pct_sequences.

XX Sequence 157 AA;

Query Match 98.2%; Score 766; DB 1; Length 157;

Best Local Similarity 94.9%; Pred. No. 0;

Matches 149; Conservative 1; Mismatches 7; Indels 0; Gaps 0;

Qy 1 VRSSRTSPDXPVAVVAVNPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 Db 1 VRSSRTSPDXPVAVVAVNPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 Qy 61 QVLFSGGCGCPSTHLLTHTTISRIVSVQTXVNLLSAIXSPCQRETPGGAEXPWYEPYIL 120
 Db 61 QVLFSGGCGCPSTHLLTHTTISRIVSVQTXVNLLSAIXSPCQRETPGGAEXPWYEPYIL 120
 Qy 121 GGVFQLEXPGRDLSAEINRPDYLDPFASGQVYFGIALL 157
 Db 121 GGVFQLEXPGRDLSAEINRPDYLDPFADDDGQVYFGIALL 157

RESULT 4

AEBA45432

ID AEB45432 standard; protein; 157 AA.

XX AEB45432;

XX 22-SEP-2005 (first entry)

XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:16.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
 XX plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 XX antiproliferative; anti-HIV; antitubercular; immunosuppressive;
 XX vasotropic; cerebroprotective; dermatological; immunomodulator;
 XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 XX mutin.

XX Homo sapiens.

OS Synthetic.

XX WO2005066206-A1.

XX 21-JUL-2005.

XX 05-JAN-2005; 2005WO-JP000032.

XX 06-JAN-2004; 2004JP-00001427.

XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.

PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.

PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;

XX WPI; 2005-506850/51.

DR N-PSDB; AEB45446.

XX Novel tumor necrosis factor TNF mutant protein, useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumor, rheumatoid arthritis, allergy.

PS Claim 4; SEQ ID NO 16; 34pp; Japanese.

XX The invention relates to tumor necrosis factor (TNF) mutant proteins, particularly tumor necrosis factor mutant proteins specific for TNF-R1 or TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses a TNF mutant protein comprising an amino acid sequence derived from the human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the N-terminus, and amino acid residues at positions 84-89 by other amino acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF mutant protein; and (2) a TNF formulation comprising a TNF mutant protein. The TNF mutant proteins are useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma), Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia, transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease, etc. The TNF mutant proteins are highly stable in vivo. This sequence represents a human TNF-alpha mutant protein specific for TNF-R1. Note: The sequence data for this patent did not form part of the printed specification, but was obtained in electronic format directly from WIPO at ftp.wipo.int/pub/published_pct_sequences.

XX Sequence 157 AA;

Query Match 98.1%; Score 765; DB 1; Length 157;

Best Local Similarity 94.9%; Pred. No. 0;

Matches 149; Conservative 1; Mismatches 7; Indels 0; Gaps 0;

Qy 1 VRSSRTSPDXPVAVVAVNPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 Db 1 VRSSRTSPDXPVAVVAVNPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 Qy 61 QVLFSGGCGCPSTHLLTHTTISRIVSVQTXVNLLSAIXSPCQRETPGGAEXPWYEPYIL 120
 Db 61 QVLFSGGCGCPSTHLLTHTTISRIVSVQTXVNLLSAIXSPCQRETPGGAEXPWYEPYIL 120
 Qy 121 GGVFQLEXPGRDLSAEINRPDYLDPFASGQVYFGIALL 157
 Db 121 GGVFQLEXPGRDLSAEINRPDYLDPFRETQVYFGIALL 157

RESULT 5

AEBA45434

ID AEB45434 standard; protein; 157 AA.

XX AEB45434;

XX 22-SEP-2005 (first entry)

XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:18.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
 XX plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;

KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.
 XX
 OS Homo sapiens.
 OS Synthetic.
 PN WO2005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX
 XX MPI; 2005-506850/51.
 DR N-PSDB; AEB45446.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 XX Claim 4; SEQ ID NO 18; 34pp; Japanese.
 PS
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;
 Query Match 97.9%; Score 764; DB 1; Length 157;
 Best Local Similarity 94.9%; Pred. No. 0;
 Matches 149; Conservative 0; Mismatches 8; Indels 0; Gaps 0;
 Qy 1 VRSSSRTPSDXPVAVHVNPAQEQQLWLNRRANALLANGVELRDNLQVPSGLYLIYS 60
 Db 1 VRSSSRTPSDMPVAVHVNPAQEQQLWLNRRANALLANGVELRDNLQVPSGLYLIYS 60
 Qy 61 QVLFPGGCPSTHLLTHTTSIRIAVSQTXNLLSAIXSPQRTPGAEAXPWPEIYL 120
 Db 61 QVLFPGGCPSTHLLTHTTSIRIAVSQTXNLLSAIXSPQRTPGAEAXPWPEIYL 120
 Qy 121 GGVLQEXGDRLSAEINRPNVDLDPAESQVYFGIALL 157
 Db 121 GGVLQEXGDRLSAEINRPNVDLDPANDQVYFGIALL 157

RESULT 6
 AEB45430
 ID AEB45430 standard; protein; 157 AA.
 XX
 AC AEB45430;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:14.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.
 XX
 OS Homo sapiens.
 OS Synthetic.
 PN WO2005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX
 XX MPI; 2005-506850/51.
 DR N-PSDB; AEB45444.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 XX Claim 4; SEQ ID NO 14; 34pp; Japanese.
 PS
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX

```
SQ Sequence 157 AA;
Query Match 97.7%; Score 762; DB 1; Length 157;
Best Local Similarity 94.3%; Pred. No. 0;
Matches 148; Conservative 2; Mismatches 7; Indels 0; Gaps 0;
Qy 1 VRSSRTPSDXPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Qy 61 QVLFPGQCPSTHVLTHTTISRIASVYQTXNLLSAXSPCQRTPEGAEXPWVEPIYL 120
Db 61 QVLFPGQCPSTHVLTHTTISRIASVYQTXNLLSAXSPCQRTPEGAEXPWVEPIYL 120
Qy 121 GGVFQLEKXGDRLSAEINRNPDLDPFASGQVYFGIALL 157
Db 121 GGVFQLEKXGDRLSAEINRNPDLDPFADKDTGQVYFGIALL 157
RESULT 7
AEB45453
ID AEB45453 standard; protein; 157 AA.
XX AC AEB45453;
XX DT 22-SEP-2005 (first entry)
XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:37.
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmadium infection; meningitis; hepatitis; Alzhaimers disease;
KW antiinflammatory; cytostatic; antiarheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-Hiv; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mitein.
XX OS Homo sapiens.
XX OS Synthetic.
XX PN WO2005066206-A1.
XX PD 21-JUL-2005.
XX PF 05-JAN-2005; 2005WO-JP0000032.
XX PR 06-JAN-2004; 2004JP-00001427.
XX PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX PA (MAYU/) MAYUMI T.
XX PA (TSUT/) TSUTSUMI Y.
XX PA (NAKA/) NAKAGAWA S.
XX PI Mayumi T, Teutsami Y, Nakagawa S, Ohta T;
Mayumi T, Teutsami Y, Nakagawa S, Ohta T;
WPI; 2005-506850/51.
DR N-PSDB; AEB45476.
XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX PS Claim 5; SEQ ID NO 37; 34pp; Japanese.
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
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CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX SQ Sequence 157 AA;
Query Match 97.3%; Score 759; DB 1; Length 157;
Best Local Similarity 94.9%; Pred. No. 0;
Matches 149; Conservative 0; Mismatches 8; Indels 0; Gaps 0;
Qy 1 VRSSRTPSDXPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Qy 61 QVLFPGQCPSTHVLTHTTISRIASVYQTXNLLSAXSPCQRTPEGAEXPWVEPIYL 120
Db 61 QVLFPGQCPSTHVLTHTTISRIASVYQTXNLLSAXSPCQRTPEGAEXPWVEPIYL 120
Qy 121 GGVFQLEKXGDRLSAEINRNPDLDPFASGQVYFGIALL 157
Db 121 GGVFQLEKXGDRLSAEINRNPDLDPFASGQVYFGIALL 157
RESULT 8
AEB45431
ID AEB45431 standard; protein; 157 AA.
XX AC AEB45431;
XX DT 22-SEP-2005 (first entry)
XX DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:15.
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmadium infection; meningitis; hepatitis; Alzhaimers disease;
KW antiinflammatory; cytostatic; antiarheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mitein.
XX OS Homo sapiens.
XX OS Synthetic.
XX PN WO2005066206-A1.
XX PD 21-JUL-2005.
XX PF 05-JAN-2005; 2005WO-JP0000032.
XX PR 06-JAN-2004; 2004JP-00001427.
XX PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX PA (MAYU/) MAYUMI T.
XX PA (TSUT/) TSUTSUMI Y.
XX PA (NAKA/) NAKAGAWA S.
XX PI Mayumi T, Teutsami Y, Nakagawa S, Ohta T;
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XX DR WPI; 2005-506850/51.
XX DR N-PSDB; AEB45445.
XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
XX PT and/or preventing diseases such as inflammation, and other diseases
XX PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX PT rheumatoid arthritis, allergy.
XX XX
XX PS Claim 4; SEQ ID NO 15; 34pp; Japanese.
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX CC a TNF mutant protein comprising an amino acid sequence derived from the
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX CC protein. The TNF mutant proteins are useful for treating and/or
XX CC preventing diseases such as inflammation, and other diseases caused by
XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
XX CC The sequence data for this patent did not form part of the printed
XX CC specification, but was obtained in electronic format directly from WIPO
XX CC at ftp.wipo.int/pub/published_pct_sequences.
XX SQ Sequence 157 AA;

Query Match 97.2%; Score 758; DB 1; Length 157;
Best Local Similarity 94.3%; Pred. No. 0;
Matches 148; Conservative 0; Mismatches 9; Indels 0; Gaps 0;

QY 1 VRSSRTPSDXPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60

QY 61 QVLFXGGGCPSTHLLTHTTISRIVSYQTQVNVLLSAIXSPCQRETPGAEAXPWYEPYIL 120
Db 61 QVLFXGGGCPSTHLLTHTTISRIVSYQTQVNVLLSAIXSPCQRETPGAEAXPWYEPYIL 120

QY 121 GGVFQLEKXGDRLSAEINRPDYLDPFASGGQVYFGIALL 157
Db 121 GGVFQLEKXGDRLSAEINRPDYLDPFASGGQVYFGIALL 157

RESULT 9
AEB45454
ID AEB45454 standard; protein; 157 AA.
XX AC AEB45454;
XX XX
XX DT 22-SEP-2005 (first entry)
XX XX
XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:38.
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX KW plasmoid infection; meningitis; hepatitis; Alzheimer's disease;
XX KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX KW antiproliferative; anti-HIV; antitumor; immunosuppressive;
XX KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
XX KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX KW muten.

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OS Homo sapiens.
OS Synthetic.
PN WO2005066206-A1.
XX 21-JUL-2005.
XX 05-JAN-2005; 2005WO-JP000032.
XX 06-JAN-2004; 2004JP-00001427.
XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
XX (NAKA/) NAKAGAWA S.
PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
DR WPI; 2005-506850/51.
DR N-PSDB; AEB45477.
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX Claim 5; SEQ ID NO 38; 34pp; Japanese.
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX SQ Sequence 157 AA;


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XX AC AEB45469;
XX DT 22-SEP-2005 (first entry)
XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:53.
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
XX KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX KW vasotropic; cerebroprotective; dermatological; immunomodulator;
XX KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX KW mutein.
XX OS Homo sapiens.
XX OS Synthetic.
XX PN WO2005066206-A1.
XX PD 21-JUL-2005.
XX PF 05-JAN-2005; 2005WO-JP000032.
XX PR 06-JAN-2004; 2004JP-00001427.
XX PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX PA (MAYU/) MAYUMI T.
XX PA (TSUT/) TSUTSUMI Y.
XX PA (NAKA/) NAKAGAWA S.
XX PI Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
XX DR N-PSDB; AEB45492.
XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
XX PT and/or preventing diseases such as inflammation, and other diseases
XX PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX PT rheumatoid arthritis, allergy.
XX PS Claim 5; SEQ ID NO 53; 34pp; Japanese.
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX CC a TNF mutant protein comprising an amino acid sequence derived from the
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX CC protein. The TNF mutant proteins are useful for treating and/or
XX CC preventing diseases such as inflammation, and other diseases caused by
XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX CC The sequence data for this patent did not form part of the printed
XX CC specification, but was obtained in electronic format directly from WIPO
XX CC at ftp.wipo.int/pub/published_pct_sequences.
XX CC Sequence 157 AA;
XX CC
XX CC Query Match 96.4%; Score 752; DB 1; Length 157;
XX CC Best Local Similarity 93.6%; Pred. No. 0;
XX CC Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;

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QY 1 VRSSRTFSDXPAHVAVANPQAEQQLWLNRRANALLANGVELRDNLVWPESEGLYLIYS 60
DB 1 VRSSRTFSDMPFAHVAVANPQAEQQLWLNRRANALLANGVELRDNLVWPESEGLYLIYS 60
QY 61 QVLFEGGCGCSTHVLTHTTISRIASVQTXXNLISAIKSPCORETPEGAEAXPWYEPYIL 120
DB 61 QVLFSGGCGCSTHVLTHTTISRTKSYSKPVNLLSARSPCORETPEGAEANPWYEPYIL 120
QY 121 GGVFLQEXGDRLSAEINRPDYLDFAESGVVFGIIAL 157
DB 121 GGVFLQEPGDELAEINRPDYLDFAESGVVFGIIAL 157
RESULT 11
AEB45438
ID AEB45438 standard; protein; 157 AA.
XX AC AEB45438;
XX DT 22-SEP-2005 (first entry)
XX DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:22.
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
XX KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX KW vasotropic; cerebroprotective; dermatological; immunomodulator;
XX KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX KW mutein.
XX OS Homo sapiens.
XX OS Synthetic.
XX PN WO2005066206-A1.
XX PD 21-JUL-2005.
XX PF 05-JAN-2005; 2005WO-JP000032.
XX PR 06-JAN-2004; 2004JP-00001427.
XX PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX PA (MAYU/) MAYUMI T.
XX PA (TSUT/) TSUTSUMI Y.
XX PA (NAKA/) NAKAGAWA S.
XX PI Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
XX DR N-PSDB; AEB45452.
XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
XX PT and/or preventing diseases such as inflammation, and other diseases
XX PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX PT rheumatoid arthritis, allergy.
XX PS Claim 4; SEQ ID NO 22; 34pp; Japanese.
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX CC a TNF mutant protein comprising an amino acid sequence derived from the
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX CC protein. The TNF mutant proteins are useful for treating and/or
XX CC preventing diseases such as inflammation, and other diseases caused by

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CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX
 SQ Sequence 157 AA;

Query Match 96.3%; Score 751; DB 1; Length 157;
 Best Local Similarity 93.6%; Pred. No. 0;
 Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;

QY 1 VRSSRTPSDXPVAHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 DB 1 VRSSRTPSDMPVAHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 QY 61 QVLFKGGCGPSTHLLTHTTISRIVSYQTXVNLLSAIXPCQRTPEGAAXPWYEPYIL 120
 DB 61 QVLFSGGCGPSTHLLTHTTISRIGPYQRPVNLLSAIXPCQRTPEGAAXPWYEPYIL 120
 QY 121 GGVFQLEPGDRLSAEINRPDYLDPAESGGVYFGIIAL 157
 DB 121 GGVFQLEPGDRLSAEINRPDYLDPAESGGVYFGIIAL 157

RESULT 12
 AEB45436
 ID AEB45436 standard; protein; 157 AA.

XX AC AEB45436;
 XX DT 22-SEP-2005 (first entry)
 XX DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:20.

XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.

XX OS Homo sapiens.
 XX OS Synthetic.
 XX PN WO2005066206-A1.
 XX PD 21-JUL-2005.
 XX PF 05-JAN-2005; 2005WO-JP000032.
 XX PR 06-JAN-2004; 2004JP-00001427.
 XX PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 XX PA (MAYU) MAYUMI T.
 XX PA (TSUT) TSUTSUMI Y.
 XX PA (NAKA) NAKAGAWA S.
 XX PI Mayumi T, Teutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 XX DR N-PSDB; AEB45450.
 XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating

PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.

XX Claim 4; SEQ ID NO 20; 34pp; Japanese.

XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, cachexia,
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 96.3%; Score 751; DB 1; Length 157;
 Best Local Similarity 93.6%; Pred. No. 0;
 Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;

QY 1 VRSSRTPSDXPVAHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 DB 1 VRSSRTPSDMPVAHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 QY 61 QVLFKGGCGPSTHLLTHTTISRIVSYQTXVNLLSAIXPCQRTPEGAAXPWYEPYIL 120
 DB 61 QVLFSGGCGPSTHLLTHTTISRIGPYQRPVNLLSAIXPCQRTPEGAAXPWYEPYIL 120
 QY 121 GGVFQLEPGDRLSAEINRPDYLDPAESGGVYFGIIAL 157
 DB 121 GGVFQLEPGDRLSAEINRPDYLDPAESGGVYFGIIAL 157

RESULT 13
 AEB45461
 ID AEB45461 standard; protein; 157 AA.

XX AC AEB45461;
 XX DT 22-SEP-2005 (first entry)
 XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:45.

XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.

XX OS Homo sapiens.
 XX OS Synthetic.
 XX PN WO2005066206-A1.

```
PD 21-JUL-2005.
PF 05-JAN-2005; 2005WO-JP000032.
PR 06-JAN-2004; 2004JP-00001427.
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Teutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45484.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 45; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
XX SQ Sequence 157 AA;
XX
XX Query Match 96.3%; Score 751; DB 1; Length 157;
XX Best Local Similarity 93.0%; Pred. No. 0;
XX Matches 146; Conservative 3; Mismatches 8; Indels 0; Gaps 0;
Oy 1 VRSSRTPSDPVAHVANPQAEQQLWLNRRANALLANGVELRDNLQVWPSGLYLIYS 60
Db 1 VRSSRTPSDPVAHVANPQAEQQLWLNRRANALLANGVELRDNLQVWPSGLYLIYS 60
Oy 61 QVLFYGGCPSHTVLLTHTTISRIVSVYCTXNLLSAIXSPCORETPEGAEAPWTEPIYL 120
Db 61 QVLFSGQGPCSTHLLTHTTISRISAYSVNLLSAIRSPCORETPEGAEANPWTEPIYL 120
Oy 121 GGVFOLEXGDRLSAENRPDVLDFAESGVVFGIIAL 157
Db 121 GGVFOLEFGDRLSAENRPDVLDFAESGVVFGIIAL 157
XX
XX RESULT 14
XX ID AEB45460
XX ID AEB45460 standard; protein; 157 AA.
XX
XX AC AEB45460;
XX
XX DT 22-SEP-2005 (first entry)
XX
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```
DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:44.
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX antiparasitic; anti-HIV; antiatherosclerotic; immunosuppressive;
XX vasotropic; cerebroprotective; dermatological; immunomodulator;
XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX mutein.
XX
XX Homo sapiens.
OS Synthetic.
OS
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
PD
XX 05-JAN-2005; 2005WO-JP000032.
PF
XX 06-JAN-2004; 2004JP-00001427.
PR
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Teutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45483.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 44; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
XX SQ Sequence 157 AA;
XX
XX Query Match 96.2%; Score 750; DB 1; Length 157;
XX Best Local Similarity 93.0%; Pred. No. 0;
XX Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;
Oy 1 VRSSRTPSDPVAHVANPQAEQQLWLNRRANALLANGVELRDNLQVWPSGLYLIYS 60
Db 1 VRSSRTPSDPVAHVANPQAEQQLWLNRRANALLANGVELRDNLQVWPSGLYLIYS 60
```

Qy 61 QVLPXGCGCPSTHVLTHTRIAVSQTXVNLISAIKSPCQRETPGAEAXPWYBPIYL 120
 Db 61 QVLPXGCGCPSTHVLTHTRIAVSQTXVNLISAIKSPCQRETPGAEAXPWYBPIYL 120
 Qy 121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157
 Db 121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157

RESULT 15
 AEB45464
 ID AEB45464 standard; protein; 157 AA.
 XX
 AC AEB45464;
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:48.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmadum infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutin.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 PN WO2005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Tautsami Y, Nakagawa S, Ohta T;
 XX
 DR WPI; 2005-506850/51.
 DR N-PSDB; AEB45487.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 XX Claim 5; SEQ ID NO 48; 34pp; Japanese.
 PS

CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID NO: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic

CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;
 Query Match 96.2%; Score 750; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;
 Qy 1 VRSSRTPSDXPAHVHVANPQAEQQLWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
 Db 1 VRSSRTPSDMPVAVHVANPQAEQQLWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
 Qy 61 QVLPXGCGCPSTHVLTHTRIAVSQTXVNLISAIKSPCQRETPGAEAXPWYBPIYL 120
 Db 61 QVLPXGCGCPSTHVLTHTRIAVSQTXVNLISAIKSPCQRETPGAEAXPWYBPIYL 120
 Qy 121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157
 Db 121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157

RESULT 16
 AEB45472
 ID AEB45472 standard; protein; 157 AA.
 XX
 AC AEB45472;
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:56.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmadum infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutin.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 PN WO2005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Tautsami Y, Nakagawa S, Ohta T;
 XX
 DR WPI; 2005-506850/51.
 DR N-PSDB; AEB45495.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 XX Claim 5; SEQ ID NO 56; 34pp; Japanese.
 PS

XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;
QY 1 VRSSRTPSDHPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVWPSGLYLIYS 60
DB 1 VRSSRTPSDHPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVWPSGLYLIYS 60
QY 61 QVLFPGQCPSTHLLTHTISRIAVSYQTVNLLSAIXSPQRETPEGAEXPWVEPIYL 120
DB 61 QVLFSGQCPSTHLLTHTISRIKSYGHPVNLLSAIRSPQRETPEGAEXPWVEPIYL 120
QY 121 GGVOLEXGDRLSAEINRPDYLDPAESGVYFGIALL 157
DB 121 GGVOLEPGDRLSAEINRPDYLDPAESGVYFGIALL 157

RESULT 17
AEB45471
ID AEB45471 standard; protein; 157 AA.
XX
AC AEB45471;
XX
DT 22-SEP-2005 (first entry)
XX
DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:55.
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzhemiers disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritis; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutin.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO200506206-A1.
XX
PD 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
PF
XX 06-JAN-2004; 2004JP-00001427.
PR

XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Teutsumi Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45494.
XX
PT Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
PS Claim 5; SEQ ID NO 55; 34pp; Japanese.
XX
CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;
QY 1 VRSSRTPSDHPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVWPSGLYLIYS 60
DB 1 VRSSRTPSDHPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVWPSGLYLIYS 60
QY 61 QVLFPGQCPSTHLLTHTISRIAVSYQTVNLLSAIXSPQRETPEGAEXPWVEPIYL 120
DB 61 QVLFSGQCPSTHLLTHTISRIYTPGVPVNLLSAIRSPQRETPEGAEXPWVEPIYL 120
QY 121 GGVOLEXGDRLSAEINRPDYLDPAESGVYFGIALL 157
DB 121 GGVOLEPGDRLSAEINRPDYLDPAESGVYFGIALL 157
RESULT 18
AEB45455
ID AEB45455 standard; protein; 157 AA.
XX
AC AEB45455;
XX
DT 22-SEP-2005 (first entry)
XX
DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:39.
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;

KW plasmodium infection; meningitis; hepatitis; antirheumatic; antiarthritic; antiallergic;
 KW antiinflammatory; cytostatic; antitumor; severe acute respiratory syndrome;
 KW antipneumonic; anti-HIV; antitubercular; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutin.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 XX W02005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 XX (MAYU/) MAYUMI T.
 XX (TSUT/) TSUTSUMI Y.
 XX (NAKA/) NAKAGAWA S.
 XX
 XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 XX N-PSDB; AEB45478.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 XX and/or preventing diseases such as inflammation, and other diseases
 XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
 XX rheumatoid arthritis, allergy.
 XX
 XX Claim 5; SEQ ID NO 39; 34pp; Japanese.
 XX
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins.
 XX Particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 XX a TNF mutant protein comprising an amino acid sequence derived from the
 XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 XX N-terminus, and amino acid residues at positions 84-89 by other amino
 XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
 XX protein. The TNF mutant proteins are useful for treating and/or
 XX preventing diseases such as inflammation, and other diseases caused by
 XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
 XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 XX The sequence data for this patent did not form part of the printed
 XX specification, but was obtained in electronic format directly from WIPO
 XX at ftp.wipo.int/pub/published_pct_sequences.

Query Match 96.0%; Score 749; DB 1; Length 157;
 Best Local Similarity 93.6%; Pred. No. 0;
 Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRRTPSDPVAHVANPQAEQQLWLNRRANALLANGVELNDQNLVPSGLYLIYS 60
 Db 1 VRSSRRTPSDPVAHVANPQAEQQLWLNRRANALLANGVELNDQNLVPSGLYLIYS 60
 Qy 61 QVLPFGQGPCSTHLLTHTISRIASVYQTQVNLISATXSPCQRTPEGAEXPWYFIYL 120
 Db 61 QVLPFGQGPCSTHLLTHTISRIASVYQTQVNLISATXSPCQRTPEGAEXPWYFIYL 120
 - Qy 121 GGVFQLEPGDRLSAEINRPDYLDFAARGQVYFGIALL 157

Db 121 GGVFQLEPGDRLSAEINRPDYLDFAARGQVYFGIALL 157
 RESULT 19
 AEB45466
 ID AEB45466 standard; protein; 157 AA.
 XX
 XX AEB45466;
 XX
 XX 22-SEP-2005 (first entry)
 XX
 XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:50.
 XX
 XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
 XX plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipneumonic; anti-HIV; antitubercular; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutin.
 XX
 XX Homo sapiens.
 OS Synthetic.
 XX
 XX W02005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 XX (MAYU/) MAYUMI T.
 XX (TSUT/) TSUTSUMI Y.
 XX (NAKA/) NAKAGAWA S.
 XX
 XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 XX N-PSDB; AEB45489.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 XX and/or preventing diseases such as inflammation, and other diseases
 XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
 XX rheumatoid arthritis, allergy.
 XX
 XX Claim 5; SEQ ID NO 50; 34pp; Japanese.
 XX
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 XX a TNF mutant protein comprising an amino acid sequence derived from the
 XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 XX N-terminus, and amino acid residues at positions 84-89 by other amino
 XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
 XX protein. The TNF mutant proteins are useful for treating and/or
 XX preventing diseases such as inflammation, and other diseases caused by
 XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
 XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 XX The sequence data for this patent did not form part of the printed
 XX specification, but was obtained in electronic format directly from WIPO
 XX at ftp.wipo.int/pub/published_pct_sequences.

```

CC at ftp.wipo.int/pub/published_pct_sequences.
XX Sequence 157 AA;
SQ
    Query Match          96.0%; Score 749; DB 1; Length 157;
    Best Local Similarity 93.0%; Pred. No. 0;
    Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;
Qy 1 VRSSRTPSDXPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
Qy 61 QVLFQXGQCPSTHLLTHTTISRIVSYQTYNLSAISXPCQRETPEGAEXPWYEPYIL 120
Db 61 QVLFSGGQCPSTHLLTHTTISRISKTYGHPVNLISAIRSPCQRETPEGAEXPWYEPYIL 120
Qy 121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157
Db 121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157
RESULT 20
AEB45474
ID AEB45474 standard; protein; 157 AA.
XX
AC AEB45474;
XX
DT 22-SEP-2005 (first entry)
XX
DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:58.
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; hepatitis; Alzheimers disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX
XX Homo sapiens.
OS
OS Synthetic.
XX
PN WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45497.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 58; 34pp; Japanese.
PS
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the

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CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
SQ
    Query Match          96.0%; Score 749; DB 1; Length 157;
    Best Local Similarity 93.6%; Pred. No. 0;
    Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;
Qy 1 VRSSRTPSDXPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
Qy 61 QVLFQXGQCPSTHLLTHTTISRIVSYQTYNLSAISXPCQRETPEGAEXPWYEPYIL 120
Db 61 QVLFSGGQCPSTHLLTHTTISRINHRYQDPVNLISAIRSPCQRETPEGAEXPWYEPYIL 120
Qy 121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157
Db 121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157
RESULT 21
AEB45457
ID AEB45457 standard; protein; 157 AA.
XX
AC AEB45457;
XX
DT 22-SEP-2005 (first entry)
XX
DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:41.
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX
XX Homo sapiens.
OS
OS Synthetic.
XX
PN WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
PF
XX 06-JAN-2004; 2004JP-00001427.
PR
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX Claim 5; SEQ ID NO 58; 34pp; Japanese.
PS
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the

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AE45458	Best Local Similarity 93.0%; Pred. No. 0;	
ID AEB45458 standard; protein; 157 AA.	Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;	
XX AC AEB45458;		
XX DT 22-SEP-2005 (first entry)		
XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:42.		
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;		
XX KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;		
XX KW acquired immune deficiency syndrome; severe acute respiratory syndrome;		
XX KW plasmoidium infection; meningitis; hepatitis; Alzheimer's disease;		
XX KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;		
XX KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;		
XX KW vasotropic; cerebroprotective; dermatological; immunomodulator;		
XX KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;		
XX KW mitein.		
XX OS Homo sapiens.		
XX OS Synthetic.		
XX PN WO2005066206-A1.		
XX PD 21-JUL-2005.		
XX PF 05-JAN-2005; 2005WO-JP000032.		
XX PR 06-JAN-2004; 2004JP-00001427.		
XX PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.		
XX PA (MAYU/) MAYUMI T.		
XX PA (TSUT/) TSUTSUMI Y.		
XX PA (NAKA/) NAKAGAWA S.		
XX PI Mayumi T, Teutsuni Y, Nakagawa S, Ohta T;		
XX DR WPI; 2005-506850/51.		
XX DR N-PSDB; AEB45481.		
XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating		
XX PT and/or preventing diseases such as inflammation, and other diseases		
XX PT caused by overexpression of TNF, such as autoimmune diseases, tumor,		
XX PT rheumatoid arthritis, allergy.		
XX PS Claim 5; SEQ ID NO 42; 34pp; Japanese.		
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,		
XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or		
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses		
XX CC a TNF mutant protein comprising an amino acid sequence derived from the		
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of		
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the		
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino		
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF		
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant		
XX CC protein. The TNF mutant proteins are useful for treating and/or		
XX CC preventing diseases such as inflammation, and other diseases caused by		
XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon		
XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),		
XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,		
XX CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute		
XX CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic		
XX CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,		
XX CC etc. The TNF mutant proteins are highly stable in vivo. This sequence		
XX CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:		
XX CC The sequence data for this patent did not form part of the printed		
XX CC specification, but was obtained in electronic format directly from WIPO		
XX CC at ftp.wipo.int/pub/published_pct_sequences.		
XX SQ Sequence 157 AA;		
XX Query Match 95.9%; Score 748; DB 1; Length 157;		

Oy	1	VRSSRTSPDXPVAVHVVANPOAEQOLWLNFRNALLANGVELRDNLVPESEGLYLIYS	60
Db	1	VRSSRTSPDXPVAVHVVANPOAEQOLWLNFRNALLANGVELRDNLVPESEGLYLIYS	60
Oy	61	QVLFSGQGCPSHVLTHHTISRIASVYOTXVNLISAIXSPCQRETPEGAAXPWYEPIYL	120
Db	61	QVLFSGQGCPSHVLTHHTISRIASVYOTXVNLISAIXSPCQRETPEGAAXPWYEPIYL	120
Oy	121	GGVFOLEXGDELRSAEINRPDYLDAESGVYFGIALL	157
Db	121	GGVFOLEXGDELRSAEINRPDYLDAESGVYFGIALL	157
RESULT 24			
AE45473	ID	AE45473 standard; protein; 157 AA.	
XX AC AEB45473;			
XX DT 22-SEP-2005 (first entry)			
XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:57.			
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;			
XX KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;			
XX KW acquired immune deficiency syndrome; severe acute respiratory syndrome;			
XX KW plasmoidium infection; meningitis; hepatitis; Alzheimer's disease;			
XX KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;			
XX KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;			
XX KW vasotropic; cerebroprotective; dermatological; immunomodulator;			
XX KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;			
XX KW mitein.			
XX OS Homo sapiens.			
XX OS Synthetic.			
XX PN WO2005066206-A1.			
XX PD 21-JUL-2005.			
XX PF 05-JAN-2005; 2005WO-JP000032.			
XX PR 06-JAN-2004; 2004JP-00001427.			
XX PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.			
XX PA (MAYU/) MAYUMI T.			
XX PA (TSUT/) TSUTSUMI Y.			
XX PA (NAKA/) NAKAGAWA S.			
XX PI Mayumi T, Teutsuni Y, Nakagawa S, Ohta T;			
XX DR WPI; 2005-506850/51.			
XX DR N-PSDB; AEB45496.			
XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating			
XX PT and/or preventing diseases such as inflammation, and other diseases			
XX PT caused by overexpression of TNF, such as autoimmune diseases, tumor,			
XX PT rheumatoid arthritis, allergy.			
XX PS Claim 5; SEQ ID NO 57; 34pp; Japanese.			
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,			
XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or			
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses			
XX CC a TNF mutant protein comprising an amino acid sequence derived from the			
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of			
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the			
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino			
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF			
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant			
XX CC protein. The TNF mutant proteins are useful for treating and/or			
XX CC preventing diseases such as inflammation, and other diseases caused by			
XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon			
XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),			
XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,			
XX CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute			
XX CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic			
XX CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,			
XX CC etc. The TNF mutant proteins are highly stable in vivo. This sequence			
XX CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:			
XX CC The sequence data for this patent did not form part of the printed			
XX CC specification, but was obtained in electronic format directly from WIPO			
XX CC at ftp.wipo.int/pub/published_pct_sequences.			
XX SQ Sequence 157 AA;			
XX Query Match 95.9%; Score 748; DB 1; Length 157;			

CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 95.9%; Score 748; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRTSPDXPVAVHVNPAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 Db 1 VRSSRTSPDMPVAVHVNPAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFPGQGCSTHLLTHTRISRIASVQTVNLLSAIXSPQRETPEGAXPWYEPYIL 120
 Db 61 QVLFPGQGCSTHLLTHTRISRIASVQTVNLLSAIXSPQRETPEGAXPWYEPYIL 120

Qy 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIALL 157
 Db 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIALL 157

RESULT 25
 AEB45467
 ID AEB45467 standard; protein; 157 AA.

XX AC AEB45467;
 XX XX
 XX DT 22-SEP-2005 (first entry)
 XX XX
 XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:51.
 XX XX
 XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.

XX OS Homo sapiens.
 OS Synthetic.
 XX XX
 XX WO2005066206-A1.
 XX XX
 XX PD 21-JUL-2005.
 XX XX
 XX PF 05-JAN-2005; 2005WO-JP000032.
 XX XX
 XX PR 06-JAN-2004; 2004JP-00001427.
 XX XX
 XX PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 XX PA (MAYU) MAYUMI T.
 XX PA (TSUT) TSUTSUMI Y.
 XX PA (NAKA) NAKAGAWA S.
 XX XX
 XX PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX WPI, 2005-506850/51.
 DR N-P8DB; AEB45490.
 DR

XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.

XX PS Claim 5; SEQ ID NO 51; 34pp; Japanese.

XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 33, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 95.9%; Score 748; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;

Qy 1 VRSSRTSPDXPVAVHVNPAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 Db 1 VRSSRTSPDMPVAVHVNPAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFPGQGCSTHLLTHTRISRIASVQTVNLLSAIXSPQRETPEGAXPWYEPYIL 120
 Db 61 QVLFPGQGCSTHLLTHTRISRIASVQTVNLLSAIXSPQRETPEGAXPWYEPYIL 120

Qy 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIALL 157
 Db 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIALL 157

RESULT 26
 AEB45468
 ID AEB45468 standard; protein; 157 AA.

XX AC AEB45468;
 XX XX
 XX DT 22-SEP-2005 (first entry)
 XX XX
 XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:52.
 XX XX
 XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.

XX OS Homo sapiens.
 OS Synthetic.
 XX XX


```

Db      1 VRSSRTPSDMPVAHVVANPQAEGLQWLNRRNALLANGVELRDNLVVPSSGLYLIYS 60
Qy      61 QVLFXGQGCPSHVLTHHTISRIASVQTXVNLISAIKSPQRETTPGAEAXPWYEPYIL 120
        : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db      61 QVLFSGQGCPSHVLTHHTISRISTTHNQPNVLLSAIRSPQRETTPGAEANPWYEPYIL 120
Qy      121 GGVFQLXGDRLSAEINRPDYLDPAESGGVYFGIIAL 157
        : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db      121 GGVFQLPGRDLSAEINRPDYLDPAESGGVYFGIIAL 157
        : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :

RESULT 28
AEB45462
ID      AEB45462 standard; protein; 157 AA.
XX      AC
XX      AEB45462;
XX      22-SEP-2005 (first entry)
XX      TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:46.
XX      tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX      autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX      acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX      plasmodium infection; meningitis; hepatitis; Alzheimers disease;
XX      antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX      antipeptidic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX      vasotropic; cerebroprotective; dermatological; immunomodulator;
XX      antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX      mutein.
XX      Homo sapiens.
XX      OS
XX      Synthetic.
XX      WO2005066206-A1.
XX      21-JUL-2005.
XX      05-JAN-2005; 2005WO-JP000032.
XX      06-JAN-2004; 2004JP-00001427.
XX      (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX      (MAYU)/ MAYUMI T.
XX      (TSUT)/ TSUTSUMI Y.
XX      (NAKA)/ NAKAGAWA S.
XX      Mayumi T, Teutsu Y, Nakagawa S, Ohta T;
XX      WPI; 2005-506850/51.
XX      N-PSDB; AEB45485.
XX      Novel tumor necrosis factor TNF mutant protein, useful for treating
XX      and/or preventing diseases such as inflammation, and other diseases
XX      caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX      rheumatoid arthritis, allergy.
XX      Claim 5; SEQ ID NO 46; 34pp; Japanese.
XX      The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX      particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX      TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX      a TNF mutant protein comprising an amino acid sequence derived from the
XX      human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX      one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX      N-terminus, and amino acid residues at positions 84-89 by other amino
XX      acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX      mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX      protein. The TNF mutant proteins are useful for treating and/or
XX      preventing diseases such as inflammation, and other diseases caused by
XX      overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX      cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX      Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,

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CC      CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC      respiratory syndrome (SARS), atherosclerosis, Bence's disease, systemic
CC      lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC      etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC      represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC      The sequence data for this patent did not form part of the printed
CC      specification, but was obtained in electronic format directly from WIPO
CC      at ftp.wipo.int/pub/published_pct_sequences.
XX      XX
SQ      Sequence 157 AA;
        Query Match          95.8%; Score 747; DB 1; Length 157;
        Best Local Similarity 93.0%; Pred. No. 0;
        Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

Qy      1 VRSSRTPSDMPVAHVVANPQAEGLQWLNRRNALLANGVELRDNLVVPSSGLYLIYS 60
Db      1 VRSSRTPSDMPVAHVVANPQAEGLQWLNRRNALLANGVELRDNLVVPSSGLYLIYS 60
        : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Qy      61 QVLFXGQGCPSHVLTHHTISRIASVQTXVNLISAIKSPQRETTPGAEAXPWYEPYIL 120
Db      61 QVLFSGQGCPSHVLTHHTISRISTTHNQPNVLLSAIRSPQRETTPGAEANPWYEPYIL 120
        : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Qy      121 GGVFQLXGDRLSAEINRPDYLDPAESGGVYFGIIAL 157
Db      121 GGVFQLPGRDLSAEINRPDYLDPAESGGVYFGIIAL 157
        : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :

RESULT 29
AEB45470
ID      AEB45470 standard; protein; 157 AA.
XX      AC
XX      AEB45470;
XX      22-SEP-2005 (first entry)
XX      TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:54.
XX      tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX      autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX      acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX      plasmodium infection; meningitis; hepatitis; Alzheimers disease;
XX      antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX      antipeptidic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX      vasotropic; cerebroprotective; dermatological; immunomodulator;
XX      antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX      mutein.
XX      Homo sapiens.
XX      OS
XX      Synthetic.
XX      WO2005066206-A1.
XX      21-JUL-2005.
XX      05-JAN-2005; 2005WO-JP000032.
XX      06-JAN-2004; 2004JP-00001427.
XX      (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX      (MAYU)/ MAYUMI T.
XX      (TSUT)/ TSUTSUMI Y.
XX      (NAKA)/ NAKAGAWA S.
XX      Mayumi T, Teutsu Y, Nakagawa S, Ohta T;
XX      WPI; 2005-506850/51.
XX      N-PSDB; AEB45493.
XX      Novel tumor necrosis factor TNF mutant protein, useful for treating
XX      and/or preventing diseases such as inflammation, and other diseases
XX      caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX      rheumatoid arthritis, allergy.

```

```
XX PS Claim 5; SEQ ID NO 54; 34pp; Japanese.
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX CC a TNF mutant protein comprising an amino acid sequence derived from the
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX CC protein. The TNF mutant proteins are useful for treating and/or
XX CC preventing diseases such as inflammation, and other diseases caused by
XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX CC The sequence data for this patent did not form part of the printed
XX CC specification, but was obtained in electronic format directly from WIPO
XX CC at ftp.wipo.int/pub/published_pct_sequences.
XX SQ Sequence 157 AA;

Query Match 95.8%; Score 747; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 0; Mismatches 11; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAHVAVNPAEQQLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVAVNPAEQQLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFPGQGCSTHLLTHTTISRIVSYQTQVNLISAIKSPQRETPEGAEXPWVEPIYL 120
Db 61 QVLFPGQGCSTHLLTHTTISRITQYSHVNLISAIKSPQRETPEGAEXPWVEPIYL 120

Qy 121 GGVFQLEKXGDRLSAEINRDPYLDFAESQGVYFGIALL 157
Db 121 GGVFQLEKXGDRLSAEINRDPYLDFAESQGVYFGIALL 157

Query Match 95.6%; Score 746; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAHVAVNPAEQQLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVAVNPAEQQLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFPGQGCSTHLLTHTTISRIVSYQTQVNLISAIKSPQRETPEGAEXPWVEPIYL 120
Db 61 QVLFPGQGCSTHLLTHTTISRIVSYQTQVNLISAIKSPQRETPEGAEXPWVEPIYL 120

Qy 121 GGVFQLEKXGDRLSAEINRDPYLDFAESQGVYFGIALL 157
Db 121 GGVFQLEKXGDRLSAEINRDPYLDFAESQGVYFGIALL 157

RESULT 31
AEB45456
ID AEB45456 standard; protein; 157 AA.
XX AC AEB45456;
XX AC AEB45459;
XX DT 22-SEP-2005 (first entry)
XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:43.
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;

Claim 5; SEQ ID NO 40; 34pp; Japanese.

The invention relates to tumor necrosis factor (TNF) mutant proteins,
particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
a TNF mutant protein comprising an amino acid sequence derived from the
human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
N-terminus, and amino acid residues at positions 84-89 by other amino
acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
mutant protein; and (2) a TNF formulation comprising a TNF mutant
protein. The TNF mutant proteins are useful for treating and/or
preventing diseases such as inflammation, and other diseases caused by
overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
etc. The TNF mutant proteins are highly stable in vivo. This sequence
represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
The sequence data for this patent did not form part of the printed
specification, but was obtained in electronic format directly from WIPO
at ftp.wipo.int/pub/published_pct_sequences.

Sequence 157 AA;

Query Match 95.8%; Score 747; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 0; Mismatches 11; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAHVAVNPAEQQLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVAVNPAEQQLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFPGQGCSTHLLTHTTISRIVSYQTQVNLISAIKSPQRETPEGAEXPWVEPIYL 120
Db 61 QVLFPGQGCSTHLLTHTTISRITQYSHVNLISAIKSPQRETPEGAEXPWVEPIYL 120

Qy 121 GGVFQLEKXGDRLSAEINRDPYLDFAESQGVYFGIALL 157
Db 121 GGVFQLEKXGDRLSAEINRDPYLDFAESQGVYFGIALL 157

RESULT 30
AEB45456
ID AEB45456 standard; protein; 157 AA.
XX AC AEB45456;
XX AC AEB45459;
XX DT 22-SEP-2005 (first entry)
XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:40.
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
XX KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX KW vasotropic; cerebroprotective; dermatological; immunomodulator;
XX KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX KW metain.
XX OS Homo sapiens.
XX OS Synthetic.
XX OS WO2005066206-A1.
XX PN 21-JUL-2005.
XX PD 05-JAN-2005; 2005WO-JP000032.
XX PF
```

KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antineoplastic; antithrombotic; antiallergic;
 KW antipneumonia; anti-HIV; antineoplastic; antineoplastic; antineoplastic;
 KW vasoprotective; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mitein.
 XX
 XX Homo sapiens.
 OS Synthetic.
 XX
 XX WO2005066206-A1.
 PN
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 DR N-PSDB; ABB45482.
 DR
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 XX Claim 5; SEQ ID NO 43; 34pp; Japanese.
 PS
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 XX Sequence 157 AA;
 SQ
 Query Match 95.6%; Score 746; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;
 Qy 1 VRSSRTPSDYPAHVANPQAEQQLWLNRRALLANGVELDNLQVPSGLYLIYS 60
 Db 1 VRSSRTPSDYPAHVANPQAEQQLWLNRRALLANGVELDNLQVPSGLYLIYS 60
 Qy 61 QVLFKGGCPTVLLTHITIRIAVSQTXNLLSAXSPQRTTPEGAEKXPMVEPIYL 120
 Db 61 QVLFKGGCPTVLLTHITIRISPLPKPNVLLSAXSPQRTTPEGAEKXPMVEPIYL 120

QY 121 GGVFQLEXGDRLSAEINRDPDYLDPAESQGVYFGIIAL 157
 DB 121 GGVFQLEPGDRLSAEINRDPDYLDPAESQGVYFGIIAL 157
 RESULT 32
 ABB45465
 ID ABB45465 standard; protein; 157 AA.
 XX
 XX ABB45465;
 AC
 XX 22-SEP-2005 (first entry)
 DT
 XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:49.
 DE
 XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antineoplastic; antithrombotic; antiallergic;
 KW antipneumonia; anti-HIV; antineoplastic; antineoplastic; antineoplastic;
 KW vasoprotective; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mitein.
 XX
 XX Homo sapiens.
 OS Synthetic.
 XX
 XX WO2005066206-A1.
 PN
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 DR N-PSDB; ABB45488.
 DR
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 XX Claim 5; SEQ ID NO 49; 34pp; Japanese.
 PS
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 XX Sequence 157 AA;
 SQ

CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 95.6%; Score 746; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 0; Mismatches 11; Indels 0; Gaps 0;
 QY 1 VRSSRTPSDYPVAHVANPOAQEQQLWLNRRNALLANGVELRDNLVPSGGLYLIYS 60
 DB 1 VRSSRTPSDMPVAHVANPOAQEQQLWLNRRNALLANGVELRDNLVPSGGLYLIYS 60
 QY 61 QVLFSGGQCPSTHLLTHTTISRIVSYQTXVNLSSAIXSPCQRETPEGAEXPWEPIYL 120
 DB 61 QVLFSGGQCPSTHLLTHTTISRITHKYPQVNLSSAIXSPCQRETPEGAEXPWEPIYL 120
 QY 121 GGVOLEKXGDRLSAENRPNPDYLDFAESGQVYFGIIAL 157
 DB 121 GGVOLEKXGDRLSAENRPNPDYLDFAESGQVYFGIIAL 157

RESULT 33
 AEB45463
 ID AEB45463 standard; protein; 157 AA.
 XX AC AEB45463;
 XX DT 22-SEP-2005 (first entry)
 XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:47.
 XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmoidium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.
 XX OS Homo sapiens.
 XX OS Synthetic.
 XX PN WO200506206-A1.
 XX PD 21-JUL-2005.
 XX PF 05-JAN-2005; 2005WO-JP000032.
 XX PR 06-JAN-2004; 2004JP-00001427.
 XX PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX FI Mayumi T, Teutsuni Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 DR N-PSDB; AEB45486.
 XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX PS Claim 5; SEQ ID NO 47; 34pp; Japanese.
 XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or

CC CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Bence's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 95.6%; Score 746; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;
 QY 1 VRSSRTPSDYPVAHVANPOAQEQQLWLNRRNALLANGVELRDNLVPSGGLYLIYS 60
 DB 1 VRSSRTPSDMPVAHVANPOAQEQQLWLNRRNALLANGVELRDNLVPSGGLYLIYS 60
 QY 61 QVLFSGGQCPSTHLLTHTTISRIVSYQTXVNLSSAIXSPCQRETPEGAEXPWEPIYL 120
 DB 61 QVLFSGGQCPSTHLLTHTTISRISRVYTPVNLSSAIXSPCQRETPEGAEXPWEPIYL 120
 QY 121 GGVOLEKXGDRLSAENRPNPDYLDFAESGQVYFGIIAL 157
 DB 121 GGVOLEKXGDRLSAENRPNPDYLDFAESGQVYFGIIAL 157
 RESULT 34
 AEB45429
 ID AEB45429 standard; protein; 157 AA.
 XX AC AEB45429;
 XX DT 22-SEP-2005 (first entry)
 XX DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:13.
 XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmoidium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.
 XX OS Homo sapiens.
 XX OS Synthetic.
 XX PN WO200506206-A1.
 XX PD 21-JUL-2005.
 XX PF 05-JAN-2005; 2005WO-JP000032.
 XX PR 06-JAN-2004; 2004JP-00001427.
 XX PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.

PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX
 DR WPI; 2005-506850/51.
 DR N-PSDB; AEB45443.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 PS Claim 4; SEQ ID NO 13; 34pp; Japanese.
 XX
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;
 Query Match 95.4%; Score 744; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 0; Mismatches 11; Indels 0; Gaps 0;
 Qy 1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLQVPSGLYLIYS 60
 Db 1 VRSSRTPSDMPVAHVANPQAEQQLWLNRRNALLANGVELRDNLQVPSGLYLIYS 60
 Qy 61 QVLFKXGQCPSTHVLTHITSRIVSVQTXVNLISAIKSPQRTPEGAEXPWYEPYL 120
 Db 61 QVLFSGGQCPSTHVLTHITSRIVSVQTPVNLISAIKSPQRTPEGAEXPWYEPYL 120
 Qy 121 GGVFQLEKGDRLSAEINRDPYLDPAESGQVYFGIALL 157
 Db 121 GGVFQLEPGDRLSAEINRDPYLDPAEQVYFGIALL 157
 RESULT 35
 AEB45428
 ID AEB45428 standard; protein; 157 AA.
 XX
 AC AEB45428;
 XX
 XX 22-SEP-2005 (first entry)
 DT
 XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:12.
 DE
 XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antithratic; antiallergic;
 KW antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;

KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.
 OS Homo sapiens.
 OS Synthetic.
 XX WO2005066206-A1.
 XX
 PD 21-JUL-2005.
 XX
 PF 05-JAN-2005; 2005WO-JP000032.
 XX
 PR 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX
 DR WPI; 2005-506850/51.
 DR N-PSDB; AEB45442.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 PS Claim 4; SEQ ID NO 12; 34pp; Japanese.
 XX
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;
 Query Match 95.3%; Score 743; DB 1; Length 157;
 Best Local Similarity 92.4%; Pred. No. 0;
 Matches 145; Conservative 1; Mismatches 11; Indels 0; Gaps 0;
 Qy 1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLQVPSGLYLIYS 60
 Db 1 VRSSRTPSDMPVAHVANPQAEQQLWNRNEHANALLANGVELRDNLQVPSGLYLIYS 60
 Qy 61 QVLFKXGQCPSTHVLTHITSRIVSVQTXVNLISAIKSPQRTPEGAEXPWYEPYL 120
 Db 61 QVLFSGGQCPSTHVLTHITSRIVSVQTPVNLISAIKSPQRTPEGAEXPWYEPYL 120
 Qy 121 GGVFQLEKGDRLSAEINRDPYLDPAESGQVYFGIALL 157
 Db 121 GGVFQLEPGDRLSAEINRDPYLDPAEQVYFGIALL 157

CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents human TNF-alpha mutant protein. Note: The sequence data for
 CC this patent did not form part of the printed specification, but was
 CC obtained in electronic format directly from WIPO at
 CC ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 95.1%; Score 742; DB 1; Length 157;
 Best Local Similarity 92.4%; Pred. No. 0;
 Matches 145; Conservative 0; Mismatches 12; Indels 0; Gaps 0;

QY 1 VRSSRTPSDXPVAHVAVNPQAEGLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
 DB 1 VRSSRTPSDMPVAHVAVNPQAEGLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60

QY 61 QVLFXGQGCPSHTVLLTHTTISRIVSYQTVNLLSAIXSPCQRETPGABAXPWYEPYIL 120
 DB 61 QVLFXGQGCPSHTVLLTHTTISRIVSYQTVNLLSAIXSPCQRETPGABAXPWYEPYIL 120

QY 121 GGVFQLEPGDRLSAEINRPPDYLDPAESGQVYFGIIAL 157
 DB 121 GGVFQLEPGDRLSAEINRPPDYLDPAESGQVYFGIIAL 157

RESULT 38
 AEB45427
 ID AEB45427 standard; protein; 157 AA.
 XX
 AC AEB45427;
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:11.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmadum infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 PN WO2005066206-A1.
 XX
 PD 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Teatsumi Y, Nakagawa S, Ohta T;
 XX

DR WPI; 2005-506850/51.
 DR N-PSDB; ABB45441.
 XX
 PT Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 PS Claim 4; SEQ ID NO 11; 34pp; Japanese.
 XX
 CC The invention relates to tumor necrosis factor (TNF) mutant proteins.
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 95.0%; Score 741; DB 1; Length 157;
 Best Local Similarity 92.4%; Pred. No. 0;
 Matches 145; Conservative 1; Mismatches 11; Indels 0; Gaps 0;

QY 1 VRSSRTPSDXPVAHVAVNPQAEGLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
 DB 1 VRSSRTPSDMPVAHVAVNPQAEGLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60

QY 61 QVLFXGQGCPSHTVLLTHTTISRIVSYQTVNLLSAIXSPCQRETPGABAXPWYEPYIL 120
 DB 61 QVLFXGQGCPSHTVLLTHTTISRIVSYQTVNLLSAIXSPCQRETPGABAXPWYEPYIL 120

QY 121 GGVFQLEPGDRLSAEINRPPDYLDPAESGQVYFGIIAL 157
 DB 121 GGVFQLEPGDRLSAEINRPPDYLDPAESGQVYFGIIAL 157

RESULT 39
 AEB45423
 ID AEB45423 standard; protein; 157 AA.
 XX
 AC AEB45423;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 XX Human TNF-alpha mutant protein, SEQ ID No:7.
 DE
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmadum infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.
 XX
 OS Homo sapiens.

```
OS Synthetic.
XX WO2005066206-A1.
XX 21-JUL-2005.
XX 05-JAN-2005; 2005WO-JP000032.
XX 06-JAN-2004; 2004JP-00001427.
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX (MAYU/) MAYUMI T.
XX (TSUT/) TSUTSUMI Y.
XX (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Teutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45424.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Example 1; SEQ ID NO 7; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents human TNF-alpha mutant protein. Note: The sequence data for
XX this patent did not form part of the printed specification, but was
XX obtained in electronic format directly from WIPO at
XX ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
XX
XX Query Match 95.0%; Score 741; DB 1; Length 157;
XX Best Local Similarity 92.4%; Pred. No. 0;
XX Matches 145; Conservative 0; Mismatches 12; Indels 0; Gaps 0;
XX
XX QY 1 VRSSRTSDYPVAHVANPQAEQOLQWLNRRANALLANGVELRDNLVVPSEGLYLYS 60
XX DB 1 VRSSRTSDMPVAHVANPQAEQOLQWLNRRANALLANGVELRDNLVVPSEGLYLYS 60
XX
XX QY 61 QVLFXGQCPSTHVLTLTHTISRIAVSYQTXVNLLSAIXSPCQRETPGEAEXPWYEPIYL 120
XX DB 61 QVLFSGQCPSTHVLTLTHTISRIAXXXXPNVLLSAIRSPCQRETPGEANPWYEPIYL 120
XX
XX QY 121 GGVFQLEKXGDRLSABINRPDYLDPAESGVQVFGIIAL 157
XX DB 121 GGVFQLEPGDRLSABINRPDYLDPAESGVQVFGIIAL 157
XX
XX RESULT 40
XX AEB45435
XX ID AEB45435 standard; protein; 157 AA.
XX
```

AC AEB45435;

22-SEP-2005 (first entry)

TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:19.

tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation; autoimmune disease; tumor; transplant rejection; cardiovascular disease; acquired immune deficiency syndrome; severe acute respiratory syndrome; plasmodium infection; meningitis; hepatitis; Alzheimer's disease; antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic; antiporotic; anti-HIV; antiarteriosclerotic; immunosuppressive; vasotropic; cerebroprotective; dermatological; immunomodulator; antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic; mitein.

Homo sapiens.

Synthetic.

WO2005066206-A1.

21-JUL-2005.

05-JAN-2005; 2005WO-JP000032.

06-JAN-2004; 2004JP-00001427.

(HAYB) HAYASHIBARA SEIBUTSU KAGAKU.

(MAYU/) MAYUMI T.

(TSUT/) TSUTSUMI Y.

(NAKA/) NAKAGAWA S.

Mayumi T, Teutsumi Y, Nakagawa S, Ohta T;

WPI; 2005-506850/51.

N-PSDB; AEB45449.

Novel tumor necrosis factor TNF mutant protein, useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumor, rheumatoid arthritis, allergy.

Claim 4; SEQ ID NO 19; 34pp; Japanese.

The invention relates to tumor necrosis factor (TNF) mutant proteins, particularly tumor necrosis factor mutant proteins specific for TNF-R1 or TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses a TNF mutant protein comprising an amino acid sequence derived from the human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the N-terminus, and amino acid residues at positions 84-89 by other amino acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF mutant protein; and (2) a TNF formulation comprising a TNF mutant protein. The TNF mutant proteins are useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma), Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia, transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease, etc. The TNF mutant proteins are highly stable in vivo. This sequence represents human TNF-alpha mutant protein. Note: The sequence data for this patent did not form part of the printed specification, but was obtained in electronic format directly from WIPO at ftp.wipo.int/pub/published_pct_sequences.

Query Match 95.0%; Score 741; DB 1; Length 157; Best Local Similarity 92.4%; Pred. No. 0; Matches 145; Conservative 1; Mismatches 11; Indels 0; Gaps 0; Sequence 157 AA;

Query Match 95.0%; Score 741; DB 1; Length 157; Best Local Similarity 92.4%; Pred. No. 0; Matches 145; Conservative 1; Mismatches 11; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPAHVAVANPQAEQQLQWLNRRANALLANGVELRDNLQVVPSSGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVAVANPQAEQQLQWLNRRANALLANGVELRDNLQVVPSSGLYLIYS 60
Qy 61 QVLFXGQGCPSHTVLLTHTTISRIVAVSYQTXVNLISATXSPCQRETPEGAEAXPWYEPYIL 120
Db 61 QVLFSGGQGCPSHTVLLTHTTISRITPAINRPNVNLISAIRSPCQRETPEGAEANPWYEPYIL 120
Qy 121 GGVFQLEKXGDRLSAEINRNPYLDPAESGQVYFGIIAL 157
Db 121 GGVFQLEKXGDRLSAEINRNPYLDPAESGQVYFGIIAL 157

RESULT 41
AEB45426
ID AEB45426 standard; protein; 146 AA.

AC AEB45426;
XX
XX
DT 22-SEP-2005 (first entry)
XX
XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:10.
XX
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antiproliferative; anti-HIV; antiartherosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; hepatotrophic; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.

OS Homo sapiens.
OS Synthetic.
XX
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.

XX (HAYB) HAYASHIBARA SEIITSU KAGAKU.
XX (MAYU/) MAYUMI T.
XX (TSUT/) TSUTSUMI Y.
XX (NAKA/) NAKAGAWA S.

XX Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45440.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.

XX Claim 4; SEQ ID NO 10; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon

CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.

XX
SQ Sequence 146 AA;

Query Match 89.5%; Score 698; DB 1; Length 146;
Best Local Similarity 93.8%; Pred. No. 0;
Matches 136; Conservative 1; Mismatches 8; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPAHVAVANPQAEQQLQWLNRRANALLANGVELRDNLQVVPSSGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVAVANPQAEQQLQWLNRRANALLANGVELRDNLQVVPSSGLYLIYS 60
Qy 61 QVLFXGQGCPSHTVLLTHTTISRIVAVSYQTXVNLISATXSPCQRETPEGAEAXPWYEPYIL 120
Db 61 QVLFSGGQGCPSHTVLLTHTTISRITPAINRPNVNLISAIRSPCQRETPEGAEANPWYEPYIL 120
Qy 121 GGVFQLEKXGDRLSAEINRNPYLDPA 145
Db 121 GGVFQLEKXGDRLSAEINRNPYLDPA 145

Search completed: September 21, 2006, 09:09:21
Job time : 1 secs